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SYPHILIS

BY

BURTON PETER THOM, M.D.

VISITING SYPHILOLOGIST TO THE HOSPITALS OF THE DEPARTMENT OF CORRECTION, WELFARE ISLAND, NEW YORK CITY

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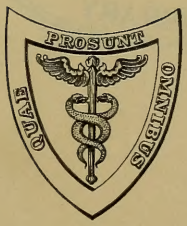

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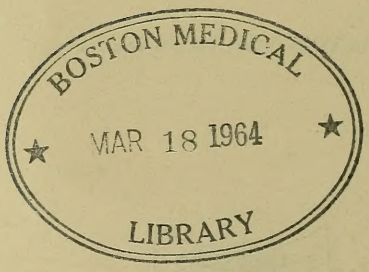

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THIS BOOK

IS DEDICATED TO

J. BENTLEY SQUIER, M.D.

AS A TOKEN OF

ESTEEM AND GRATITUDE

"I have been accused of seeing syphilis everywhere,
but I am afraid I have not seen it often enough."

PHILIPPE RICORD

FOREWORD.

In the past, and in the present also to some extent, syphilis has been considered almost entirely as a skin disease; although since the days of John, of Vigo, it has been known that syphilis attacks the parts beneath the skin. The isolation of the Treponema pallidum as the cause of syphilis, and the practical application of the phenomenon of complement-fixation by Wassermann, Neisser and Bruck as a means of diagnosis, have vastly changed our conception of syphilis as a pathologic entity. The astute clinicians of a generation or two ago spoke of parasyphilis and metasyphilis in describing conditions which they surmised, but could not prove, to be of syphilitic origin. The work of Noguchi, Moore, Warthin and many others has proved that they were right. Only the prefixes that they used were wrong; there is no parasyphilis or metasyphilis; there is only syphilis in whatever guise it chances to appear. Tabes, paresis and the degenerative changes in the heart, bloodvessels and other viscera are as frankly syphilitic as is the chancre or the roseola.

The dermatoses of syphilis are but passing incidents in its evolution. If they were the sum of its problems their solution would not be difficult. As much and more is syphilis a neuropathy and a visceropathy. There is no organ or tissue that is exempt from its attack. The surgeon can ignore it no more than the internist or other specialist.

Syphilis is discussed here as it confronts the physician in his work of every day. I have tried, as far as in me lies, to tell much that we now know about syphilis—to tell all would be impossible—and I have tried to tell it simply so that the reader can come by the facts contained herein easily and quickly.

The teacher who presents something useful does much; the teacher who brings out what is useful does more. If the reader

can be made to think of syphilis as the frequent underlying cause of many obscure conditions; if he can be brought to realize that syphilis more than any other disease is the simulator, not to say the originator, of many degenerative syndromes which on their face are not related to it; if he can be made to think of syphilis when otherwise he would not, and to treat it boldly and intelligently, which is the only way it should be treated—if, by reading this book, it will so impress his mind, it will have served its purpose well.

BURTON PETER THOM.

NEW YORK CITY,
JULY, 1922

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SYPHILIS.

CHAPTER I.

HISTORY OF SYPHILIS.

For some reason which I have never been quite able to understand, every text-book on syphilis contains a more or less extended reference to the history of the disease. The subject possesses interest not only to the medical historian but to the physician in active practice whose chief interest lies in anamnesis rather than in ancient lore.

Origin of Syphilis.—Whoever studies the history of syphilis soon comes in contact with two opinions as to the origin, or rather the original habitat of the disease (for how it originated we do not know), and how it became endemic throughout the world. One of these opinions is that syphilis is indigenous to the Western Continent, and was brought to Europe by the sailors of Columbus. The other view is that the disease is of prehistoric origin and was in evidence among all of the races of antiquity, and that its sudden appearance in Europe shortly after the discovery of America was but a coincidental recrudescence. The writings of Bloch have popularized the former view, in this country at least. But it is with the latter that I am in accord. I believe the disease to be most ancient, and of world-wide incidence.

Derivation of the Word Syphilis.—The word syphilis is undoubtedly derived from the two Greek words, *σύν, with*, and *φιλεῖν, to love*. From this its venereal origin is obvious. It was first used by Hieronymus Fracastor, an Italian physician, in a Latin poem entitled "Syphilis, or the French Disease," published at Verona in 1530. Fracastor tells the story of a shepherd named Syphilus who insulted the god, Apollo, who avenged himself on the unfortunate youth by afflicting him with the disease, "which the inhabitants of the country called the disease of Syphilus."

Antiquity of Syphilis.—That syphilis existed in the stone age or before has been proven conclusively by Parrot. His conclusions were later confirmed by Broca, Virchow, Rollet, Quatrefages and

others. The earliest historic mention of syphilis is to be found in the Chinese medical treatise called the Nuei-King, which the Emperor Hoang-Ti caused to be compiled more than twenty-six centuries before the Christian era. In the Ebers Papyrus, which is contemporary with Sesostris, the great Egyptian warrior king, who flourished in the fifteenth century B.C., a disease is described which is undoubtedly syphilis. Cuneiform inscriptions on the clay tablets, forming the library of Assur-Ban-I-Pal, King of Assyria, indicate that the disease was well known to the Assyrians and Babylonians long before Abraham lived in "Ur of the Chaldees."

FIG. 1.—Girolamo Fracastoro (1484–1553). (Garrison.)

That syphilis was prevalent among the Jews in the Mosaic period there is no reason to doubt, if we consider the Biblical texts in the light of modern knowledge. Centuries before Guatama Buddha sat beneath the grateful shade of the sacred Bo tree, the Hindoos were acquainted with syphilis and, what is more, used mercury to cure it. In the third book of *Epidemics*, Hippocrates describes a disease which can be none other than syphilis. The Romans, Galen and Celsus, and the Alexandrian, Dioscorides, describe a disease which is without a doubt of syphilitic origin. The Latin poet Martial writes of a "shameful" contagious disease, the so-

called ficosis or fig-like disease. He describes how the disease may spread through an entire household because of the immorality of its members. The "figs" of Martial were undoubtedly condylomata lata. Horace also, in some of his jovial poems, derides those who are afflicted with ulcers because of their lubricity. The symptoms, as described by these ancient writers, are those of only one disease—syphilis.

In the middle ages the same evidences are found. The writings of the monkish medical chroniclers, Theodoric, Lanfranc, Salicet and Gerard, attest to this. It has been assumed by some that in mediæval times syphilis and leprosy were more or less confounded. If we analyze this assertion, however, it will be seen that leprosy was an exotic disease and stood out sharply among other affections; whereas the lesions produced by syphilis were not always included in this category. As the investigator into the history of syphilis goes backward in time, he comes to a period when leprosy was a universal scourge in Europe. But he also finds that true leprosy was even then a well-defined disease entity, apart and different from other skin diseases of severe type.

Historians of the new school seek only the truth. They realize the futility of the indirect method of historical research. Their efforts therefore are directed largely to the examination of documentary evidence on the subject. In regard to syphilis most of the evidence belongs to the latter half of the sixteenth century. These documents show that a disease identical with syphilis was prevalent throughout Europe at least fifty years—which is as far back as most of them go—before Charles de Bourbon besieged Rome in 1494, when the disease was supposed to have become epidemic. It may be well to note, in passing, that in connection with de Bourbon's famous siege, data recently brought to light throw grave doubt upon the authenticity of the venereal outbreak said to have taken place in his army, which was supposed to have caused the disease to spread throughout the civilized world. The names "morbus gallicus" and "malla frantzos," which came into general use, shortly after, were even then by no means new. The "French disease" seems to have been the original name for syphilis in certain countries long before the French army invaded Italy. In other countries words in use for syphilis originally meant a pustular eruption; for example, Spanish "bubas;" French, "la verole;" English, "pokis." Just why syphilis received the name of the "French disease" is unknown. Even so that was the name given to it by the barbers of Paris in documents dated in 1490.

Syphilis and Farcy.—The descriptions of the pestilence that decimated the army of Charles read very much like an account of farcy. The detailed accounts that have come down to us agree

far better with the description of acute and chronic farcy than they do with syphilis. Confusing syphilis with farcy was not uncommon among physicians of the time. Indeed, a theory then extensively believed was that the disease originated by soldiers copulating with glandered mares. It is perhaps of more than coincidental significance that an epidemic of glanders existed among the horses of the French army during the campaign.

That syphilis was present among the red aborigines when the Spaniards came to America is undoubtedly true. The bones from pre-Columbian graves offer conclusive evidence of the fact. But that by no means disproves that it was not known in Europe. Rather does it strengthen this view; for ethnologists now agree that the red men are derived from an East Asiatic stock and as Asia is a part of the world where syphilis is of the highest antiquity it is not difficult to understand the incidence of the disease among them before the discovery of Columbus.

The first to describe syphilis with any degree of exactness was John de Vigo (born 1460). He has left a good, if brief, description of chancre of the penis and of the vulva. Jean Forel (1496–1558) was the first to insist that a lesion of the epidermis was necessary for the introduction of the causative organism into the system. But it was not until more than a century later that an accurate description of syphilitic lesions of the internal organs was given by the great Italian pathologist, Morgagni.

John Hunter (1728–1793).—A name famous in the annals of syphilis is that of John Hunter, an Englishman whose description of the primary lesion—the chancre—stands as a classic to this day. But it must be said that quite as good a description of the chancre had already been given by André, a contemporary of Hunter. The fame of Hunter has been clouded by his promulgation of the now obvious error that gonorrhea, syphilis and chancroid are each different expressions of the same disease. Balfour, Hales, Ellis, Tode and Duncan disagreed with Hunter at the time and held views more in accord with modern concepts, but except to the few their names are now unknown. The correction of Hunter's mistake, which, strange as it may seem to us of the present, long held sway, was the work of Philippe Ricord, the greatest syphilologist of his time—the early and middle nineteenth century. The names of Stoll, Plenck, von Rosenstein and Sanchez must not be omitted. Their original observations in the important field of hereditary syphilis still hold good although they were published nearly two hundred years ago.

Philippe Ricord.—Philippe Ricord (1799–1889) was the greatest authority on venereal diseases after Hunter. Not only did he demolish the false theories of Hunter, which had deluded two

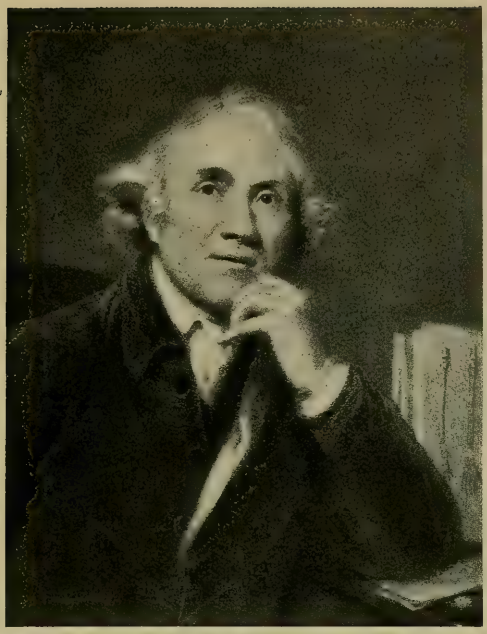

FIG. 2.—John Hunter (1728-1793). (Courtesy of the British Journal of Surgery, 1913–1914.)

FIG. 3.—Philippe Ricord (1799–1889). (Garrison.)

generations of medical men, but he also was the first to recognize and classify the three stages of the disease—primary, secondary and tertiary. He also brought potassium iodide into common use in the treatment of the later phases of syphilis; although the honor of first introducing this important remedy belongs to William Wallace, of Dublin who first used it in 1836. Ricord is credited with a vast number of clever, if *risqué*, maxims pertaining to venereal disease. Dr. Oliver Wendell Holmes styled him "the Voltaire of pelvic literature—a skeptic as to the morality of the race in general, who would have submitted Diana to treatment with his mineral specifics, and ordered a course of blue pills for the vestal virgins."

Rudolph Virchow.—One of the first as well as one of the foremost of the new age of scientific medicine was Rudolph Virchow (1821–1902). He was preëminently a pathologist and he delved deeply into the mysteries of syphilis. He was the first to throw light upon the peculiar periods of latency and recrudescence of the disease and he established the fact of the passage of the infective agent into the blood from the different organs and tissues. Wallace and von Waller proved that secondary syphilis was contagious, which had been long denied by Ricord. Clerc and Rollet were the first to investigate the different types of chancre.

Modern Names.—When the science of bacteriology became established, mainly through the efforts of Pasteur, many workers devoted themselves to the discovery of the organism causing the disease. None of them succeeded until Schaudinn and Hoffmann, of Berlin, working together, discovered the Treponema pallidum in 1905. In 1907 Wassermann demonstrated the diagnostic test which justly bears his name. In 1910 Paul Ehrlich (1854–1915) gave salvarsan to the world, and in consequence will always rank as one of the supreme masters of the healing art. Since then Hideyo Noguchi, a Japanese, of the Rockefeller Institute, has done much to explain many of the problems of syphilis of the nervous system, and Swift and Ellis working under the same auspices, by a unique application of Ehrlich's great remedy, have brought about a marked advance in the treatment of syphilis of the nervous system.

Some day—and it is not, I think, far distant—the last page in the history of syphilis will be written. Slowly but surely the disease is being conquered. Soon it will pass, and then will be lifted the heaviest curse that ever banned the sons of men.

CHAPTER II.

EXPERIMENTAL SYPHILIS.

Hunter's Work on Syphilis.—The great John Hunter was the pioneer in experimental syphilis. In 1767 he inoculated himself with the disease and thereafter studied it as it became manifest in his own person. Despite the fact that he was a keen and shrewd observer and possessed a first-rate medical mind he reached the conclusion that syphilis, gonorrhea and chancroid are but different manifestations of one disease. For that reason his work is valueless today and he is remembered chiefly by his classical description of the chancre—the so-called "Hunterian sore." Hunter also believed secondary syphilis to be non-contagious. The prestige of his name caused these errors to continue for a long time, and it was not until sixty years later that the illustrious Ricord proved their fallacy.

Ricord's Work on Syphilis.—Ricord demonstrated by inoculation experiments on man that gonorrhea and syphilis are two distinct disease entities. He experimented chiefly by inoculating recent syphilitics with their own products, the material being taken from both primary and secondary lesions. From chancre he obtained over 1000 positive results, but in 518 experiments with material from secondary lesions the results were always negative. In consequence thereof, he made the quite natural mistake of assuming that secondary syphilis was not contagious. At this period, however, it must be remembered that the distinction both as to cause and effect, which we now know to exist between the hard and the soft sore was not so well recognized; and there is no doubt that much of the material used by Ricord was obtained from chancroid rather than from chancre. The ease with which a soft sore could be inoculated led to many experiments on syphilitics and non-syphilitics. The false views then held regarding the identity of the two diseases led to the practice of "syphilization," which consisted in repeated inoculations of a syphilitic with material from chancroid under the impression that immunity would result thereby. The principle was the same as that enunciated by Jenner in vaccination for variola—the vaccine therapy of the present day.

Chancre and Chancroid Distinguished.—It was not until 1862 that the difference between the two venereal ulcers—chancre and

chancroid—was definitely determined, and this distinction was not complete until 1889 when Unna and Ducrey discovered the streptobacillus which we now know to be the specific cause of chancroid. During the period of Ricord's activity in experimental inoculation, that is, from 1835 to 1862, his example was followed by many others. The material used was obtained from the chancre, mucous patch, blood, pus or from any lesion available to the experimenter. The total number of successful inoculations recorded in the reports of the time does not seem to have been large. Levaditi states them to have been 27 in all. When we consider the number of experimenters engaged and the long period of time over which their experiments extended, to me this seems to be a rather slight showing, particularly when the highly contagious nature of the disease is taken into consideration.

Experimental Syphilization of Animals.—In 1864 Auzias-Turenne, who may be said to have been the first to practise experimental syphilization of animals, succeeded in successfully inoculating a cat. But it must be said in passing, that the success of his achievement was open to grave doubt. This line of investigation was at once taken up by others and many different domestic animals were used. The pig seemed to be the favorite and so continued even until the discovery of the Treponema pallidum.

As long ago as 1879, Klebs experimented with monkeys. He inoculated a piece of chancre subcutaneously and while no primary lesion followed, regional adenopathy and an eruption of confluent papules appeared. Nodules in the kidney and pleura were observed at postmortem. It is more than probable that he succeeded in transmitting the disease. Three years later Martineau and Hamonic undoubtedly obtained a positive result, but no follow-up tests were made. The work of these three investigators caused others to follow but as these later ones obtained only negative results the work fell into abeyance for a long time.

It is well to note, however, that there is a subtle, but none the less real, connection, as it were, between the results obtained by these older investigators and those whom we class as modern. This is to be found in the fact that the degree of inoculability of syphilis depended largely upon the species of simian used for the purpose. Thus, in 1886, Sperk inoculated a large number of monkeys but only in the *Macacus* did he obtain a positive result. Again, in 1893, Maurice Nicolle obtained positive results only in this species of monkey. His brother Charles, working along similar lines, in spite of a somewhat elaborate technic succeeded in obtaining only incomplete positive results. He published his studies in 1903. Hamonic also reported some new results in the same year.

In the same year, 1903, Metchnikoff and his co-worker, Roux, experimented on a chimpanzee—the first instance of an anthropoid ape being used for this purpose. They obtained absolute clinical results, which were followed by proofs of transmissibility and histological evidence as well. Neisser, Finger and Lassar now took up the work and in a comparatively short time a full knowledge of syphilis as it occurs in the anthropoid ape was established. Shortly after this Neisser, accompanied by several collaborators, journeyed to Java and conducted his researches in the original habitat of the chimpanzee. It was not long thereafter that he demonstrated conclusively that the chimpanzee always gives a positive result when inoculated with syphilis and that the disease runs practically the same course as in man. The period of incubation was found to be from two to seven weeks, with an average of four weeks. The chancre was reproduced exactly as in man. Also, as in man, it healed without treatment in about two months. In some of the animals a phagedenic stage was noted which Neisser ascribed either to the virulence of the infection or as a part of the exacerbation of the secondary stage. This phagedenism partook of the character of the serpiginous syphilide in man. The average time between the appearance of the chancre and the eruption was slightly over a month. The eruption showed as a roseola or as a papulo-squamous syphilide with occasional mucous patches. Strange to relate, Neisser does not record any severe constitutional reactions such as not infrequently occur in man. Autopsy findings were of no special interest except enlargement of the spleen. In a few of the animals paraplegia developed, and all of these recovered. No tertiary lesions were recorded—possibly because the animals did not live long enough.

Another simian which has been extensively experimented upon is the orang. This animal, while it develops the primary lesion and the adenopathy, never shows any further evidence of the disease. The reason for this is undoubtedly due to the fact that it receives the infection in an attenuated form, as it were, which is, perhaps, proof that it belongs to a lower evolutionary type than the anthropoids, yet it is higher than some other species of simians which are rebellious to inoculation with syphilis.

Primary Lesion.—The primary lesions artificially produced in the *Macacus* and other lower monkeys have been studied in detail. Thus we know that in them the period of incubation is considerably shorter than in the anthropoids. The clinical features also show much variability. For instance, induration as a rule is slight. In monkeys lower than the chimpanzee the primary lesion is never so characteristic; yet it faintly shows all of the clinical features of the typical sore as it occurs in man. In the

lower monkeys the secondary phagedena which Neisser observed is not seen; occasionally, however, a secondary gangrenous infection develops, which is sometimes fatal. Also, in the lower monkeys adenopathy is rare. From these facts it can be asserted, without fear of contradiction, that in the lower monkeys secondary syphilis does not develop despite the scattered claims of some investigators.

In so far as other animals are concerned, the rabbit has been inoculated in the eye and in the testicle and the tissue removed from the resulting lesion has been used to produce a similar lesion in another animal, thus proving its infectivity. There is no reason to doubt that syphilis could be produced in other animals of species remotely divergent from man and the simia. In passing, I might add that in rabbits the period of incubation is very much longer than the time required to produce the same lesion in the lower monkeys.

Susceptibility of the Skin to Inoculation.—One of the interesting discoveries made in experiments on animals is the fact that the susceptibility of the skin to inoculation is not everywhere the same. This is noted, however, in those animals whose inoculability is low, as in the inferior simians. In the chimpanzee, as in men, all regions are inoculable. In the *Cynocephalus* monkey the disease is inoculable only in the skin of the abdomen; while in the *Macacus* a positive inoculation can only be obtained in the eyebrow or in the free border of the eyelid. The reason for this difference of degree in inoculability is not known. Neisser believed it to be due to a difference in the vascularity of the parts. He observed in the young *Macacus*, that although the skin of the eyebrow is thinner, it is more difficult to inoculate than when the animal is older. In the older animal the vascularity is greater and from this Neisser assumed the reason for vascular difference. There is also considerable difference of susceptibility according to the depth of the inoculation. The epidermis and the layers immediately beneath it are more susceptible for the growth of the treponema than the deeper dermal layers. Finger obtained positive results by subdermic inoculations in small pockets after ordinary methods had failed. His idea was that in this manner he could establish a nidus of the disease as it were. His idea can be better understood if we realize that inoculations were not made with treponemata freshly obtained from a syphilitic lesion or from a culture of such, because a considerable period of time elapsed before this was done, as the causative organism had not yet been discovered.

Subcutaneous Injections.—Attempts to produce the disease by subcutaneous injections were unsuccessful. In 51 cases Neisser obtained negative results in every one. He, however, obtained

some results which were, to say the least, somewhat paradoxical. He first inoculated subcutaneously and then after some delay injected in other animals emulsions of the organs of the animals first injected. Most of these secondary injections resulted negatively but he obtained in some instances results which might be termed positive. Neisser and Levaditi are in accord in explaining why subcutaneous injections give negative results. Their explanation is simple. It is that the treponemata are overwhelmed by the natural forces of the body, or in other words by the process of phagocytosis. To prove his contention Neisser prevented leukocytosis in a monkey and then inoculated the animal by injecting subcutaneously an emulsion of syphilitic material. Constitutional syphilis ensued.

Neisser also learned that the testicle can be inoculated as readily as the eye in certain animals, notably rabbits. Since then with improved technic the number of special organs which can be directly inoculated has been increased; although the eye and the testicle are the parts most frequently used.

It is claimed that when rabbits are inoculated in the testicle the primary lesion may show considerable variety of type according to the strain of treponema. This statement has been made by first-class authorities, but I am inclined to dispute it as I cannot bring myself to recognize "strain" in treponemata. I admit that it is possible; but I desire to go on record as not believing it probable.

The constitutional lesions following testicular inoculation in the rabbit are of interest. I will first mention lesions of the different structures of the eye. Among these are choroiditis and neuroretinitis, keratitis and lesions involving the peri-cornea; cyclitis and cataract resulting therefrom have also been noted. Diagnosis with the ophthalmoscope is extremely difficult and repeated examitions are required before a satisfactory conclusion can be reached.

The nose is also attacked. Small tumors of the nasal passages occur which sometimes increase in size sufficiently to seriously embarrass respiration. In these cases the nasal discharge was found to contain treponemata. Other constitutional lesions noted were paronychia and mucous patches on the penis and its sheath.

It has been asserted by Reasoner and others that the treponemata have a certain predilection for the nervous system of rabbits with manifestations which closely parallel those in man. Noguchi, who has also extensively investigated the subject, does not agree with him. His opinion is quite to the contrary, in that he believes that the nervous system of the rabbit is particularly refractory to the influence of the treponemata.

Syphilis in the Rabbit.—Syphilis in the rabbit was first studied by Uhlenhuth and Muller in 1909–1910. From 1910 to 1914 Nichols

and Reasoner took up the work at the Rockefeller Institute. During this period Nichols and Reasoner studied 73 rabbits representing 32 generations. They found that the primary lesion in the testicle of the rabbit was not of the true chancrous type but rather a circumscribed orchitis, nodulated and showing a tendency to involve the tunica vaginalis and to undergo central necrosis. They also, in a few cases, noted metastatic involvement of the other testicle. Although most of the cases were as just described, yet not a few showed the clinical characteristics of the true chancre. The average incubation period was found to be thirty-nine days, and the lesions remained palpable for a period averaging one hundred and five days. In three-fourths of the cases inoculated involvement of the fundus oculi occurred. On the whole, while differing somewhat, the results of the Americans agreed with those of their predecessors, Uhlenhuth and Muller.

Incubation Period in Animals.—The period of incubation in animals is of great interest. Authorities differ as to what constitutes an incubation period; this is because of its variability. Finger considers it to end at the first evidence of the initial lesion; and with his opinion I am in accord. On the other hand, Neisser places it at the end of the period when there is no question of the lesion being specific. From this standpoint it would seem to me that they both agree, insomuch as it is understood that the lesion is to be regarded as specific. Finger, and the workers in the Pasteur Institute, give the period in the higher simians as thirty days and in the lower as twenty-three days. No distinction as to the genus of the animals used is made by Neisser; he arranges them in groups according to the lengths of the incubation period. In Neisser's series most of the animals developed a chancre in from twenty-six to thirty days, but in a large percentage the period was from thirty-one to forty days. The limit was between fifteen and sixty-five days.

In considering these figures it is interesting to note the similarity in the time-length of the incubation period in animal and human syphilis. This similarity was noted by Fournier and Auspitz. Where differences occur it is important to determine the reasons therefor. One interesting fact is that those animals which are most refractory to inoculation have the shortest period of incubation. Metchnikoff's explanation of this incubation variability was that the tissues in certain instances offered greater resistance to the invading organism. With his theory I am in accord. Neisser believed that the length of the incubation period was determined by the number of treponemata which gained entrance at the initiatory portal. With the object of proving his theory, he inoculated eight *Macacus* monkeys with material from a single human chancre

and watched the results. It is to be noted that the animals were of the same species, and the virulence of the infecting material was constant. In all of the animals the incubation period was unusually long—from forty-three to fifty-eight days. This long period of incubation he explained to his own satisfaction by the fact that each animal received only a minimum number of the infecting organism. My own opinion is that while it is possible that the number of the infecting organisms may play a role in the length of the incubation period, the susceptibility of the host is the factor most to be considered.

Neisser also made some interesting experiments in aborting the chancre by excising the inoculated area. For this purpose he chose six monkeys which had been inoculated simultaneously and excised the area of inoculation after a few minutes, a few hours and several days. In each instance the chancre was aborted, even in the one longest delayed—twelve days. He repeated the experiment but in each instance the chancre developed. Thus the second series of experiments nullified the first. It would seem to me from this, that what we term incubation must have only a relative significance. It is evident that a very brief interval elapses when the treponemata begin to diffuse themselves from their portal of entry. This diffusion may be inherent in the organism itself or it may be due to agencies within the body. It is probable that both factors are at work.

The question whether the treponema undergoes an evolutionary cycle within the body before it can exert its pathological action cannot, as yet, be answered. I am well aware that McDonagh has answered the question in the affirmative, to his own satisfaction, at least; but I am not yet ready to accept his conclusions.

It is worthy of note that rabbit syphilis can be produced by intravenous injections without the development of a primary lesion. The same can also be produced in man—the so-called syphilis d'emblée. In rabbits the constitutional symptoms sometimes appear before the chancre; which means, in this instance, that the chancre is a by-product as it were, although it may represent a local defense.

Antibodies.—Zinsser, Hopkins and McBurney, by passing treponemata through several generations of rabbits, succeeded in developing antibodies. The report of these workers lends new interest to the subject of immunity. It is one which has long engaged the attention of syphilologists. More than fifty years ago Belhomme inoculated a scrofulous individual four times in succession with the serum of a chancre. The dates of inoculation were October 5, 6, 11 and 12; the chancres appeared November 10, 14 and January 10 and 21. Lindwurm inoculated a prostitute

on the right thigh at three different points and a few days later on the left arm. The incubation period for the thigh was nineteen days and for the arm twenty-four days. Puech inoculated a man with carious bone disease with pus from a six weeks' old chancre on the abdomen. Twenty-two days later he made a second inoculation in the same locality with serum obtained from a chancre twenty days old. Positive results followed both inoculations; but while the incubation period of the first inoculation was thirty-nine days, the duration of the second was only seventeen days.

The results of these experiments show that no complete immunity is conferred during the incubation of the chancre. They also show how rapidly the treponemata are diffused after inoculation. In Puech's case the susceptibility seems to have been even increased.

These early investigators, however, by no means exhausted the subject. Finger experimented on a *Rhesus* monkey—making the first inoculation on December 7, and the second on December 16. On December 21 the signs indicated that the first inoculation was taking, and on December 26 the same was true of the second. From this it will be seen that not only was the second incubation shorter but it was also noted that the second lesion was not so pronounced and healed more rapidly. Hence the contention of Puech was partly upheld, in that the first inoculation gives rise to a certain amount of protection; although there is at the same time what might be termed a certain amount of sensitization also, on account of which the period of the second incubation is not so prolonged. In five of Finger's cases the average period of incubation was not quite twenty days in the first inoculation and less than thirteen days in the second. Neisser made a series of inoculations on simians of both high and low types with an average of forty-eight days after the first inoculation and forty days after the second.

Immunity to Second Inoculation.—At least sixteen early experimenters have proven conclusively that immunity to a second inoculation with syphilis develops shortly after the first inoculation. This also proves, I might add, that the autoinoculability of the chancre is for only a short and definite period. Recently considerable work has been done along these lines. Queyrat reported a number of experiments in 1904. He selected a man having multiple primary lesions, the dates of their appearance having been ten, nine and four days before. He took material from each and made separate inoculations on the same day. Twelve days later one of the inoculations showed inflammatory changes but its appearance was by no means that of a typical chancre. It partook more of the character of a squamous papule. It was followed by regional adenopathy. In fourteen other experiments similar results

were obtained, which was plainly proof that a certain degree of immunity was acquired. Queyrat's conclusions were that the individual infected with syphilis remained autoinoculable from ten to twelve days after the appearance of the first chancre. His experiments also confirmed the older teaching that the second incubation is shorter than the first. He also observed that in the inoculations subsequent to the first sore the second was never a typical chancre.

This leads us to consider another form of experiment—the irritation of the skin in old syphilis to provoke active lesions. Tarnowsky was the pioneer in this as far back as 1877. Many years later Neumann also devoted his attention to it. Chemical, thermal and other irritants were used. In some of the experiments the subject was in the midst of an outbreak of late generalized lesions. The lesions induced resembled those produced by Queyrat, that is, they were not at all typical.

Queyrat later made further experiments. Well acquainted as he was with the work of Tarnowsky, Neumann and others, in his later work he practised sterile control traumatisms. The majority of these, however, gave only negative results. That is, the positive results from the actual inoculations were undoubtedly due to the presence of the treponemata in the inoculating material and not to those present in the body of the host. He noted also that the lesions produced by inoculation were more typical the nearer they were in point of time to the appearance of the chancre.

These findings have been confirmed by similar experiments on monkeys. At the Pasteur Institute it was shown that this stage of refractoriness to further inoculation begins some time after the activity of the inoculation chancre is manifest. It is expressed by non-receptivity to further inoculation. However, the limits of this period could not be fixed; and this caused Finger and Neisser to investigate it. Finger made a series of experiments on reinfection in 9 *Macacus* monkeys. He obtained 6 positive results and concluded that reinoculation could be effected during the first five days subsequent to the appearance of the chancre. At the Pasteur Institute the corresponding interval was ten days. In these experiments it was noted that the chancres produced by reinoculation were less fugacious and had a shorter period of incubation than the original lesion. When the period of second inoculability had expired the majority of the animals were immune to further inoculations, as is the case in human beings, except in very rare instances; exceptions to this rule, however, were noted. Thus, a *Cynocephalus* monkey was reinoculated ten months after the first inoculation, with an incubation period of nine days. The lesion was not typical and disappeared completely within a month.

Neisser reinoculated 37 simians of different types and obtained positive results. In these the incubation period was prolonged, as in Finger's experiments, the average was almost a month.

In monkeys, as in man, spontaneous recurrences take place either upon the original chancre or close to it, thus simulating in animals the chancre redux as it occurs in human syphilis. These recurrences may appear even while the original sore is in a state of evolution. Metchnikoff and Roux were the first to note this phenomenon and were absolutely convinced of its syphilitic nature. Finger also confirmed the existence of these lesions. They resemble typical chancre with a serpiginous tendency and when healed leave a pigmented scar. Neisser also obtained a series of these local recurrences which in his series appeared shortly before the chancre had completely healed.

The nature of these recurrent lesions is obscure. It cannot be said that these new foci are the result of the general infection. When they appear in animals they are immune to further inoculation and I think the same may be said of human beings. It cannot be doubted that they are due to a local propagation of the treponemata, which, as the organisms diffuse themselves from their original focus cause a local reinfection to occur, or rather infection in localities which have not yet developed immunity. From this it would seem that the tissues develop immunity by piecemeal as it were.

Neisser also discovered some important and pertinent facts by a series of experiments on monkeys killed just at the time when skin immunity developed. He showed that the viscera of such animals can still convey the disease by inoculation. This was especially marked in material for inoculating purposes taken from the bone marrow. In this respect syphilis shows a remarkable resemblance to the piroplasmoses and trypanosomiases. Neisser thus demonstrated that although immunity corresponds with and is dependent upon the development of antibodies in the blood, the organisms still lurk in the remote recesses of the body which can thereby be made to convey the disease. It is to be noted, therefore, that immunity in syphilis is only partial and is more or less limited to the skin and mucous membranes. Something like this is seen in vaccination for variola, in which after immunity has developed it is limited only to the skin, and even the cornea can be made to take the infection.

The skin immunity does not exist before the appearance of the primary lesion nor for a number of days afterward. When the tertiary stage of the disease is reached it yields somewhat, but it is then rather a refractory state than a true loss of immunity. Finger made a special study of such tertiary accidents as they

may be termed, and demonstrated that when they are produced by treponemata introduced from without the resemblance to lesions caused by treponemata from within the body was complete, and also that both differed from primary and secondary lesions. It is plainly evident that this phenomenon cannot arise from different strains of treponema. It must, therefore, be due entirely to a difference in the reaction of the tissues. Also, it must be inferred that this difference must proceed wholly from regional or relative immunity. The mechanism of this process we do not at present understand.

Metchnikoff endeavored to immunize monkeys by inoculating them with dead or sterile material. His work was carried out on the higher simians. His experiments were not successful. Finger experimented with the lower simians, using material sterilized by heat; Neisser employed other methods of sterilization, but neither obtained positive results. Metchnikoff continued the experiment by using attenuated treponemata. He first took material from a chancre in a *Macacus* monkey, which, as is well known, does not show the constitutional symptoms of the disease. This he inoculated into a chimpanzee and obtained after fourteen days a slight lesion without induration or adenopathy. Allowing an interval of thirty days to elapse he reinoculated the animal with material from a human chancre but no lesion developed after a long period of observation. From this it would seem that passage through a lower animal weakened the infective power of the treponemata and gave them the force of a vaccine as it were. However, neither Neisser nor Finger was willing to recognize this. Both of them experimented with that object in view but were unable to observe any attenuation in the infectivity of the treponemata. Likewise, some of the experiments made at the Pasteur Institute showed that passage through several animals did not attenuate the infecting power of the treponemata. Metchnikoff now experimented with spirochetal material that had been passed through 22 *Macacus* monkeys. By so doing he shortened the incubation period to seven days. With this attenuated material he inoculated a chimpanzee and obtained a negative result. He then determined to make a crucial experiment on a human being. A man, aged seventy-nine years, was inoculated, also a *Macacus* and a chimpanzee for control purposes. In the human subject the inoculation failed to take, although two slight papules, without adenopathy, which soon passed away, did appear. It cannot be stated whether they were specific or not. The chimpanzee developed a typical chancre with constitutional symptoms and the *Macacus* developed a slight primary lesion.

Vaccination Against Syphilis.—In recent years considerable experimental work has been done in vaccination against syphilis, thus reviving what had been tried long ago. The idea originated in the Pasteur Institute to immunize prostitutes with living treponemata; but to what extent it was tried, or with what results, I am unable to say. Krause, of Vienna, endeavored to treat the disease after the manner of the Pasteur treatment for rabies. His method differed very little from the older methods which had already been tried without success. He administered his vaccine while the patients were still in the primary stage. The injections were given subcutaneously. Twenty patients were treated before the secondary symptoms appeared and controls were supplied. None of them gave evidence of any reaction. In a certain number the appearance of the exanthem was notably delayed. In 7 no exanthem whatsoever appeared. From this Krause concluded that his method was preventive in about one-third of the cases. Other observers, unfortunately, could not corroborate his conclusions.

Finger prepared an emulsion of chancres and lymph nodes which he injected five or six weeks after infection. His results were negative in every instance. Other workers obtained similar results, including Metchnikoff who tried Krause's method on a chimpanzee.

Serotherapy.—In the domain of serotherapy much experimental work has been done on animals in the effort to discover a serum that would cure the disease. Such work is by no means new, but the results achieved and the technic employed by the older workers need not be detailed here, while the work of comparatively recent date has never been checked up. In the older research the animals used were the horse, ass, dog and goat—animals not known to develop the disease, or at least, extremly resistant to it. The work done at the Pasteur Institute was along modern scientific lines. Here it was soon demonstrated that syphilis could neither be prevented nor cured by this means. The workers at the Pasteur Institute clearly proved that if infective material was introduced into an animal such as a higher or lower simian and was followed by injections of serum, the disease process which the former inaugurated was not modified. But it was also proved that if syphilitic blood be injected into a monkey there is no doubt that antibodies are formed, which is determined by the fact that the serum obtained from the blood of the animal possesses distinct spirillocidal power. An example of this was noted when a mixture of fresh infective material and serum containing antibodies when inoculated into a lower simian failed to produce the disease; while in a control animal injected with the same material without the spirillocidal serum, a chancre appeared after the usual period of incubation.

Prophylaxis.—Prophylaxis against syphilis also belongs under the head of experimental work. To Mechnikoff and his confrères in the Pasteur Institute belongs the honor of first demonstrating the successful application of this procedure, for it is not new. Long ago it had been tried. Massa, in the sixth chapter of his *De Morbo Gallico*, advocated bathing the penis after suspicious coitus with white wine and vinegar. Lime juice was also used. Fracastor, in his poem from which syphilis derives its name, celebrated the use of a prophylactic. Fallopius advised a liquid preparation of mercury and guaiac. Guilbert de Preval, in 1772, prescribed a lotion of distilled water, lime water, alcohol and bichloride of mercury. For his pains, his name was stricken from the list of the regent doctors of the Paris Faculty. John Hunter also suggested the use of bichloride solution. In 1828 Coster devised a chlorinated lotion which received the enthusiastic approbation of the great Ricord.

The first to originate a method approaching that now in use was Behrman, of Nuremburg, in 1900. He advocated the frictional application of gray mercurial ointment as a prophylactic measure. He advised that the parts exposed should be well rubbed for several minutes with from 3 to 5 gm. of the ointment as soon after contact as possible. Cohn, of Berlin, suggested a modification of Behrman's method, which consisted in the application *before* coitus of an ointment composed of Lederman's mercurial ointment to which resorcin had been added. *After* intercourse he advised washing the parts with mercurial soap.

When the widespread incidence of syphilis is considered it would seem that none of the methods described were attended with any degree of success. When it was discovered, however, that the higher and lower monkeys could be inoculated with syphilis, the study of prophylaxis from a scientific basis naturally followed. The subject was taken up in a systematic way by Metchnikoff and his colleague, Roux. They had already ascertained that the treponemata are easily destroyed by moderate heat—a temperature of 48° C. for half an hour being sufficient to destroy the organism *in vitro*. This led them to believe that prolonged heating of the inoculated point might prevent the disease from developing *in loco*. They, therefore, inoculated a monkey on the penis and an hour later immersed the animal's organ in warm water gradually heated to 48° C. The immersion at this temperature was kept up for forty minutes. The result was negative. They next tried bichloride solution but with no better results. They then began experimenting with mercurial ointments. A chimpanzee was inoculated on both eyebrows with material obtained from two human beings each having a chancre. Three-quarters of an hour

later the inoculated areas were rubbed for ten minutes with double strength mercurial ointment (mercury, 100 gm., benzoinated lard, 100 gm). The result of this treatment was that no chancre developed; although another chimpanzee which had been inoculated the same day with the same material, and to which no preventive treatment had been applied, developed a chancre. To make assurance doubly sure, the chimpanzee to which the preventive ointment had been applied was inoculated forty days later with material obtained from a human chancre; within a month the animal developed syphilis. This proved to their satisfaction that the treponemata from the first inoculation had been destroyed by the mercury without giving immunity to a subsequent inoculation of syphilis.

They found mercurial ointment to be too irritating and they then had recourse to calomel ointment which they found to be the ideal prophylactic. When their results became known, objections were raised that a simian is not entirely comparable with man, and for that reason it could not be positively affirmed that the same result would be obtained in preventing human syphilis. It was, therefore, proposed that Metchnikoff and Roux inoculate themselves and then apply the prophylactic treatment. After some hesitation they agreed. But before they did so, they waited for the result of an inoculation made on Maisonneuve, a student of the Faculty of Paris. This inoculation, which was treated with the calomel ointment, did not result in syphilis.

Since that time—1906—the use of calomel ointment has become the recognized prophylactic against syphilis. Its use is now compulsory in the armies of all civilized nations, and as its value becomes better known to the laity at large it is possible and probable that the incidence of syphilis will be much reduced.

It is the consensus of opinion that during the secondary stage, and for a protracted period in the tertiary stage, the bodily organism is refractory or immune to further infection. But it has been observed in rare cases that reinfection can occur. Usually when it did occur it was manifest only by the primary lesion and limited ganglionic involvement. Cases of this kind have been reported since the time of Diday.

Reinfection.—The first attempt to settle definitely this question of reinfection by experiment was made by Finger in 1906. The result of his work was to prove that absolute immunity during either the secondary or tertiary stage of syphilis does not exist. Finger observed the following phenomena: If chancrous material is inoculated in subepidermic pockets, squamous and even crustaceous syphilides will develop in about two weeks. These when healed leave pigmented scars. At a later period of the secondary

stage the lesions produced were less pronounced. During the tertiary stage inoculations were found to produce lesions resembling those of the tertiary stage. In this connection it is to be noted that the inoculations were made with material from primary and secondary lesions and the lesions produced were typical tubercular syphilides, ulcers and gummata, such as would be found in the tertiary stage of the disease. Control experiments made with heat-killed treponemata proved beyond doubt that the lesions produced were caused by the living treponemata.

In regard to the relative infectivity of syphilitic products, much information exists. In the chimpanzee it has been noted that the papulo-squamous syphilides, mucous papules and chancre are all readily inoculable. The lymph nodes, not only those near to the primary lesion, but those which are also remote, can be used to transmit the disease, showing the universal extension of the organisms through the lymphatic system. Before Finger's experiments it was commonly believed that the lymph nodes contained no infectious material and consequently were not contagious.

Somewhat prior to Finger's experiments Salmon, of the Pasteur Institute, had made similar experiments. He inoculated *Macacus* monkeys with material from a gumma of a human being with negative results. The control animals, which were inoculated with material from secondary lesions, developed chancre. Finger, however, obtained quite different results from material obtained from a human gumma. With this material he inoculated a *Cynocephalus* monkey on the eybrow and at the end of twenty days he obtained a typical chancre. The animal, in this instance, was immune to inoculation from secondary material. Neisser and his associates confirmed Finger's findings in so far as the inoculability of closed gummata were concerned. With ulcerating gummata they obtained only negative results. However, other investigators succeeded in inoculating a monkey with material from the margin of a gummatous ulcer.

Strange as it may seem, inoculation with the type of syphilis which is most virulent—precocious malignant syphilis—has been negative. The treponemata must be undoubtedly present in these fulminant lesions, yet it would seem from these results that they are not present in excessive numbers. From this it is to be inferred that this type of the disease is due to lack of resistance rather than to the excessive virulence of the infecting organism.

Syphilis is Constitutional.—Clinical experience teaches us that syphilis is constitutional from the time of the appearance of the initial lesion. Recently Brown and Pearce of the Rockefeller Institute have conclusively demonstrated on rabbits that the disease is constitutional within a few hours after infection. It remains for

experiment to show how this occurs. Neisser made experiments by inoculating blood and tissues during the period of incubation. He demonstrated that by the fifth day the blood may be infectious, *i. e.*, blood taken from one animal previously inoculated with syphilis could be used to inoculate another. He discovered also that twenty-three days is the maximum time during which this can be done. He also found that material taken from the spleen could inoculate the disease as early as fourteen days after the inoculation of the animal from which the material was taken. Propagation through the lymphatics was demonstrated by the discovery of the organisms in the lymph nodes. This, however, was known before the infectivity of the blood was known. The knowledge of this fact is due to Hoffmann, who found the treponemata circulating in the blood stream.

Since we are aware of the course and action of the organisms during the active stage of the disease, the question naturally arises what becomes of them during the period of latency when no symptoms are manifest, a phenomenon which nearly always occurs in the course of the disease and which was first recognized by Virchow.

Neisser, in his work on the higher apes during his sojourn in Java, was able to throw much light on this subject. He discovered that the organs capable of being used for inoculating purposes were the spleen, bone-marrow, lymph nodes and testicles. He also noted that in the lower simians, which do not develop the constitutional symptoms of the disease, the same organs harbor the treponemata and that it was even easier to recover the treponemata from the organs of the lower simians than from the higher. He discovered also that some of these organs were infectious two hundred and eighty-three days after inoculation. In passing, I may say that the early and persistent presence of the treponemata in the testicle, if investigated further, would, in my opinion, throw considerable light upon the possibility of exclusive paternal syphilis and the infection of women by impregnation.

As long ago as 1851 Waller inoculated a human being with syphilitic blood. Thirty-four days later a chancre appeared. From the modern point of view his work was open to criticism in that no attention was paid to asepsis. Waller made 3 such experiments, 2 of which were attended with positive results. Julius Bettinger, who published his work anonymously in 1855, made 6 inoculations with blood taken from syphilitics, with 3 positive results. The 3 cases in which positive results were obtained were in good previous health with the exception that they all 3 had varicose veins of the legs. It is rather peculiar to note in these cases that, while constitutional lesions developed, there was no primary lesion.

Lindwurm injected blood from a pregnant syphilitic woman

under the skin of a woman suffering with carcinoma. A primary lesion developed in four weeks and this was followed by secondary symptoms. The result obtained in this case is further worthy of note by reason of the fact that it has been demonstrated at the Pasteur Institute that subcutaneous inoculations are always attended with negative results. Pellizzari inoculated with syphilitic blood 3 medical students with their consent, and obtained 1 positive result. Of these 13 inoculations of human beings with blood from syphilitic individuals, 7 positive results were obtained. The results of these early investigators have since been confirmed by results obtained with monkeys carried out by various workers and by methods more nearly approaching the scientific ideal than was possible or thought of by the workers of a former time.

It had long been surmised that the semen of a syphilitic person was infective, but the fact had never been proven by experiment. In 1876–1877 Mireus inoculated the semen of a man with syphilis into 4 subjects. In each instance he used a different technic, but all 4 results were negative. No further experiments are known to have been made until 1905 when Finger and Landsteiner inoculated successfully a *Cynocephalus* monkey with the semen of a man who had recently acquired syphilis. The technic employed was somewhat elaborate. The semen was obtained by milking the seminal vesicles and the prostate and was inoculated into subdermal pockets on the pubis and eyebrow—the primary lesion appearing on both locations. The usual test of a second inoculation was made and the animal was found resistant.

Hoffmann, Neisser and others equally experienced were not able to obtain these results. The reason for their non-success, however, may have been because they inoculated with semen obtained from individuals with tertiary syphilis. The summary of these results would indicate that the semen in recent syphilis is not always infectious, and in late syphilis rarely if ever so.

Infection of the Cerebrospinal Fluid.—The infectivity of the cerebrospinal fluid was formerly doubted, but experimental inoculations on rabbits with cerebrospinal fluid withdrawn from patients with tabes, paresis and cerebral syphilis by Uhlenhuth and Mulzer, Nichols and Hough, Hoffmann and others have been successful in producing chancres in these animals. Similar results were obtained by Artzt and Kerl with cerebrospinal fluid withdrawn from patients in the early stage of syphilis and in whom there were no clinical evidences of involvement of the nervous system. The cerebrospinal fluid used in the experiments of Artzt and Kerl was negative to the Wassermann reaction although the blood of these patients was positive in every instance. Fruhwald and Zaloziecki were also able to produce syphilis in rabbits by using cerebrospinal

fluid withdrawn from syphilitics free from symptoms pointing to involvement of the nervous system. In the subjects, however, from whom the cerebrospinal fluid was obtained, the blood was in every instance positive, although the cerebrospinal fluid was not positive in every instance.

Positive Wassermann reactions have been obtained with the milk of syphilitic women by Bab, Bar and Daunay, Thomsen and Rojas. Uhlenhuth and Mulzer obtained positive results in rabbits by inoculating the testicles with the milk of syphilitic women.

The exudates and transudates of syphilitics have been studied by Roger and Sabareanu, Jacquet and Durand, Wile and Riser. Fluid obtained from blisters, joints, pleural fluid, ascitic fluid, pericardial fluid and fluid from edema obtained with Southey's tubes was in nearly every instance positive to the Wassermann reaction.

CHAPTER III.

THE MICROBIOLOGY OF SYPHILIS.

The Treponema Pallidum.—Syphilis is caused by a specific organism—the Treponema pallidum; also called, but not so correctly, the Spirocheta pallida. To Schaudinn and Hoffmann, belongs the honor of first isolating it as the cause of syphilis. This was in 1905 and since that time it has been studied perhaps more than any other organism, except possibly the tubercle bacillus, so that now our knowledge of it may be said to be fairly complete. It fulfils Koch's postulates, and it has been found in all of the lesions of syphilis in every stage of its development. It is found in greater numbers in the primary and secondary lesions than in tertiary lesions; and in active congenital syphilis it is found more frequently and more abundantly than in the acquired form.

There is no organ or tissue of the body which it does not invade, except perhaps the enamel of the teeth; and it shows a special predilection for lodging in the lymphatic glands and for circulating in the lymph channels. It has been found in the blood stream in the secondary stage by Bandi and Simonelli and by Levaditi and Petresco. While it attacks indiscriminately any and every organ of the body, it seems to show a tendency to attack the walls of the bloodvessels and the tissues of the cerebrospinal axis. It is held by some that there are neurotrophic and dermatotrophic types of the organism; that is, one which attacks almost exclusively the skin and mucous membranes and another which shows a similar affinity for the nervous system. I do not believe this view to be correct, but believe that the lesions produced by the organism, in whatever part of the body they may appear, depend entirely upon the power of resistance of that part.

The length of the Treponema pallidum varies from 6 μ to 20 μ, although longer ones have been reported. Its transverse measurement is so minute that it is hardly possible to determine it. The shape of the organism is most delicate and it is but slightly refractive. Its form is spiral with many undulations and these vary from 3 to 12 or more, and are more angular and sharply defined than those observed in other treponemata. This spirality is present not only when the organism is in motion but also when it is at rest. Whether it has an undulatory membrane or not is still a

matter of dispute. I am inclined to believe that it has. The vitality of the Treponema pallidum is very low. It dies quickly when moisture is absent, and in the presence of moisture it is kept alive only with great difficulty; it is also difficult to cultivate it on artificial media. When examined in fresh preparations it is extremely motile—gliding and rotating upon its long axis. It is still undecided whether it is a bacterium or a protozoön, and if it divides by longitudinal or transverse fission. In my opinion the evidence leans toward its being a protozoön and that it divides transversely.

FIG. 4.—The two spirochetes in the center are Treponemata pallida; the three others, Spirocheta refringens. (Schaudinn and Hoffmann.)

The Treponema pallidum cannot be stained with the weaker anilin dyes, and even the strongest, such as carbol fuchsin and gentian violet, stain it only faintly and unsatisfactorily. The Treponema pallidum can be observed alive in the hanging drop or under a cover-glass that has been rimmed with vaseline. The lesion to be examined is first thoroughly washed with distilled water and sterile gauze. Part of the base and margin is then scraped with a curette until the superficial tissue is removed and blood appears. The blood is wiped away with sterile gauze until clear serum begins to ooze. A drop of this serum is used for examination. It is most important in preparing specimens of treponemata from chancres or lymphatic glands to obtain the material from the deeper tissues so that the specimen will not be contaminated with other organisms; and it should also be as free from

blood as possible. The specimen should be examined with a dark-field illuminator which is screwed in the place of the Abbé condenser. An arc light should be used. The preparation is made upon a slide and protected with a cover-slip. A drop of oil is placed upon the upper surface of the dark chamber, and the slide is placed upon it so that there is an even layer of oil, free from air bubbles. It should be examined with a high-power dry lens. The highly refractive cell bodies stand out against the black background, causing the motility of the organisms to be plainly noticeable.

Examination of Smears.—The examination of smears is made in the following manner. Make a smear on a slide or cover-slip, being careful to have the specimen as free from blood as possible. Fix in methyl alcohol for ten to twenty minutes and then dry. Cover the specimen with a freshly prepared solution of the following:

Distilled water	10.0 cc
Potassium carbonate (1:1000)	0.9 "

To this add 10 or 12 drops of Giemsa's solution. The staining fluid is allowed to remain for three or four hours. The specimen is then washed in running water, blotted and mounted. The organisms are stained a violet-red color. If the smear is thick the organisms may be made to come out a little more clearly by dipping in 50 per cent methyl alcohol before washing in water; then the washing need not be so thorough. By this method the cytoplasm stains blue and the nuclear substance a blue-red or azure.

A much more rapid method, and one equally as accurate, is the following: Fix the smear with methyl alcohol as before and flood with azure I solution. Then drop on an aqueous solution of eosin until an iridescent pellicle begins to appear. It takes only about fifteen or twenty minutes to prepare a specimen by this method.

Owing to the inequality of manufacture I do not recommend Goldhorn's stain. Staining by the India-ink method is both rapid and accurate. Bacteria do not grow in the ink, and cotton fibers and other détritus can be readily distinguished from the treponemata. A drop of serum is obtained in the manner already described and immediately mixed with a drop of Günther India ink. The mixture is then spread by using the edge of another slide after the manner employed in examining stained-blood specimens. The smear thus prepared quickly dries and is then examined with an oil immersion lens. The Treponema pallidum is seen unstained on a black background.

Tissue Sections.—Ordinary histological staining methods do not show the treponema in tissue sections. For staining tissues, in

order to detect the treponema, I advise Levaditi's modification of the Ramon y Cajal silver stain. By this I do not mean pyridin Levaditi stain, which is much quicker but not so accurate.

A section 1 to 2 mm. in thickness is cut from the tissue to be examined and hardened in a 10 per cent formalin solution for twenty-four hours. It is then washed and hardened in 96 per cent alcohol for twenty-four hours, after which it is washed in water until the tissue sinks. It is then impregnated with silver by soaking it for three to five days in a 2 or 3 per cent solution of nitrate of silver at a temperature of 38° C. When removed from the silver solution it is washed quickly in water and allowed to stand for one or two days at room temperature in:

Acid pyrogallic	4 gm.
Formalin	5 cc
Distilled water	100 "

When the tissue is taken out of this solution it is washed and dehydrated in absolute alcohol and mounted in paraffine. Do not cut the sections thicker than 5 mm. Stain with Giemsa stain for a few minutes and wash in water, then in alcohol containing a few drops of oil of cloves; clear in xylol and mount in balsam. The treponemata appear as black, non-refractive bodies clustered about the bloodvessels and only rarely penetrating into the cellular parenchyma.

I would not advise the amateur pathologist to diagnose by means of tissue sections. It is work requiring knowledge and training. The search for treponema in fresh serum is not, however, so difficult, although considerable experience is necessary before anything like accuracy can be secured. It must also be remembered that there are other organisms resembling the Treponema pallidum which may be present to confuse the novice. Especially, the Spirocheta dentium which is found in the mouth; the Spirocheta vincenti which is present in Vincent's angina; the Spirocheta balanitidis which Hoffmann and Prowazek assert is the cause of balanitis. From the localities from which these spirochetæ are obtained, and the lesions which they produce, it can be readily understood how easily mistakes in diagnosis can be made. In this regard I cannot do better than quote the words of Edward L. Keyes. "Unhappily it is to be foreseen that, as spirocheta diagnosis assumes greater and greater prominence in the diagnosis of syphilis, the tribe of near pathologists will feel fully competent to pass upon this—the most delicate point—in the diagnosis of the most important infectious diseases that afflicts mankind; to the cocksure diagnosis of the hasty practitioner will be added the scientific diagnosis of incompetence."

CHAPTER IV.

PROTOZOAL INFECTIONS OTHER THAN SYPHILIS.

The study of the more important protozoal diseases which, because of their origin, bear a more or less close analogy to syphilis, is important in arriving at a better understanding of the pathological evolution of the latter. An attempt will be made in this chapter to consider these analogies.

The pathology and clinical expression of a disease are determined by the nature of its exciting cause. For that reason, syphilis in all of its protean aspects must be due entirely to the action on the tissues of the body of the Treponema pallidum. As an infecting agent this holds, as it were, a unique position among microörganisms. For, while on the one hand, it possesses the pathogenic attributes of the protozoa, on the other it shares with the bacilli group the faculty of causing granulomata.

The Treponema pallidum is able to cause a chronic inflammation of the nervous system—meningo-encephalitis. The only other organism which can produce this effect is also a protozoan—the trypanosome which causes sleeping sickness. But the analogy of syphilis to other protozoal diseases does not end there. Its tendency to repeat itself by successive outbreaks, after seeming quiescence, is also a characteristic of protozoal disease as exemplified by chronic malaria. The general adenopathy, in which the exciting organisms are lodged, is also paralleled by the trypanosomic disease, sleeping sickness and Chagas's disease, or South American trypanosomiasis. Between syphilis and frambœsia or yaws the analogy is closer still. The protean character of the Treponema pallidum is but slightly greater than that of Treponema pertenue. Further, it is stated by good authority that yaws may attack the nervous system in a manner similar to syphilis.

Another, and quite as important analogy, is the response which syphilis shares with protozoal diseases to antimony, mercury and arsenic; quinine, the sovereign specific in malaria, alone having no effect upon its course.

In so far as it produces granulomata, which ulcerate and destroy, the Treponema pallidum closely resembles the tubercle bacillus, the Bacillus lepræ, the Bacillus mallei and perhaps others. Clinically it can, and not infrequently does, imitate all of the diseases produced by these bacilli.

In addition to these analogies, syphilis is still further a disease unique and apart. No other infection is so transmissible by heredity or so interferes with reproduction. No other disease has such a selective action on the bloodvessels unless we except the selective action of Chagas's disease on the cardiac musculature.

It is not possible, therefore, to fully understand the nature of syphilis in all its varied phases without a knowledge of the basic type of affection to which it belongs. It was formerly believed that the organisms, which caused these similar affections, must, of necessity, be closely allied and that they were animals, because vegetable organisms such as bacteria do not act after the manner of the protozoa. But at present the opinion is gaining ground that the organism of syphilis may, after all, prove to be a vegetable. For that reason if no other, I must ask the reader to waive for the time being, at least, the point of biological resemblance between these organisms.

The diseases which are caused by this group are essentially chronic and relapsing and are able to exist in the tissues in a quiescent state for a considerable period of time, only to react and inaugurate a fresh outbreak of the disease.

Since the various analogies between these diseases have not been worked out, they can only be given in a fragmentary manner. One thing, however, has been noted by all observers, and that is their susceptibility to chemotherapy, and in particular to arsenic and its congener, antimony. These substances, when administered therapeutically, seem to be able to reach and destroy the infecting organisms wherever they may be located in the body.

Tuberculosis.—We know that tuberculosis is a bacterial infection and that for long periods it can lie dormant, yet it not infrequently becomes active again and gives rise to acute processes, but the conditions produced by the two types of disease—syphilis and tuberculosis—one caused by a protozoön and the other by a bacillus—show notable differences which will appear in detail as we proceed.

Tubercle bacilli circulating in the blood can cause a fatal bacteriemia, or again they may lodge in some organ like the kidneys or the bone-marrow and cause local lesions; but repeated explosions followed by subsidence do not occur as is the case in syphilis. The tubercle bacillus also cannot be reached by chemotherapy, despite what the future may hold. The treponemata and trypanosomes have an affinity—a special predilection would express it better—for the nervous system, which the tubercle bacillus does not have, although at times it does produce meningitis.

Our knowledge of the analogy of syphilis to protozoal diseases, in so far as chemotherapy is concerned, began with the introduction

of atoxyl in the treatment of sleeping sickness—a disease caused by a trypanosome. It must be noted, however, that years before this it was known that arsenic exerted a favorable influence upon the disease. Ehrlich and Bertheim first produced the combination of arsenic and anilin which has since become known as atoxyl. The new drug was first used in medical practice by F. Blumenthal in 1902. He asserted that it was forty times less toxic than liquor potassii arsenitis or Fowler's solution. Thomas, of Liverpool, was the first to introduce it in the therapy of trypanosome diseases. Thomas and Breinl obtained excellent results in the experimental infection of rats, mice and rabbits with the trypanosomes of surra, nagana and sleeping sickness. Experiments conducted by Mesnil, Nicolle and Ehrlich were not so favorable. Working independently of Thomas, they administered the drug to animals infected by the tsetse-fly—surra and mal de caderas. The drug was also tried by Kopke, Broden, Rodhain and others in the treatment of sleeping sickness. But it was Robert Koch, the discoverer of the tubercle bacillus, who first undertook the systematic use of the drug in the treatment of sleeping sickness in Africa where he had journeyed to be where he could command a large amount of material. Koch proved that within eight hours after the injection of atoxyl, the trypanosomes had already disappeared from the lymphatic glands and the blood. Along with the disappearance of the organism a distinct improvement in the patient's condition took place.

Dourine.—Following upon Koch and encouraged by him, Uhlenhuth began a series of investigations at the Imperial Health Institute in Berlin, in 1906, in the treatment of dourine with atoxyl. Dourine is a trypanosome disease of horses and is transmitted by sexual intercourse. It was once common throughout Europe, but at present is more or less confined to Northern Africa and parts of North America. The symptoms of the disease are expressed by swelling of the genitals, edema of the abdomen, eruptions and adenopathy. The animal becomes progressively emaciated, with profound anemia, and paralyses develop, chiefly of the posterior extremities.

The disease can be readily transmitted to small animals such as are used for laboratory purposes. By infecting rats, the blood from them furnishes any amount of trypanosomes for research at short notice. The laboratoty disease is rather a blood state than a disease with local manifestations. The infected rat blood is injected directly into a vein and in a few days the horse's blood will contain the organisms in large numbers. Three days later an acme, as it were, is reached, which is followed by a rapid decline until the blood in a few days more is comparatively sterile. Uhlen-

huth soon discovered that atoxyl would destroy the organisms in the blood. He also noted that in the laboratory form of the disease the eruptive manifestations and paralysis present in the natural form of the disease are not so marked. Dourine and sleeping sickness show so many points of analogy, especially in laboratory results, that the question arises if they are not the same disease.

Fowl Spirillosis.—The cause of fowl spirillosis is the Spirillum gallinarum which was discovered by Marchoux and Salimpeni, of Rio de Janeiro, in 1903.

The organisms can be detected in the blood on the second day after infection. They rapidly increase up to the fourth to sixth day, when they can be found in the blood in large convoluted agglomerations. On the seventh to the ninth day the crisis of the disease occurs. The spirochetæ then disappear from the blood spontaneously and the animal either dies or is henceforth immune.

After thoroughly investigating dourine, Uhlenhuth transferred his activities to fowl spirillosis and the action thereon of atoxyl. This disease, which is common to the domestic fowl, is a septicemia attended with fever and diarrhea, followed later by somnolence and generalized weakness and paralysis of the legs or wings or both. It ends in death or recovery. Emaciation and profound cachexia do not necessarily mean death, which when it does occur is caused by convulsions. The spirilla are found in the blood. Uhlenhuth used atoxyl as a prophylactic and curative measure. As a prophylactic he injected the drug and a culture of the organism at the same time and found that infection could thereby be prevented for a considerable period of time. He showed that the arsenic acts by increasing the formation of antibodies and stimulating the defensive action of the leukocytes. He also proved that the drug acts directly on the parasites but that its spirillocidal power was not great and cure, therefore, was slow. It does not produce a sudden sterilization. Uhlenhuth wrote a paper on the results of his work, in 1911, in which he states his opinion that Ehrlich did not give him credit for priority in his investigations.

Hata, the Japanese associate of Ehrlich, also took up the investigation of the spirillose disease, the disease of fowls—recurrent fever and syphilis. He began with recurrent fever and by inducing the disease in rats and mice was able to abort and cure it with the arsenical preparation which later became famous as salvarsan. Before arriving at this, however, he tried out various other arsenical compounds. He noted in this disease that it was possible to render it so virulent that the remedy was of no avail. He was equally successful in fowl spirillosis. Finally he treated rabbit syphilis with arsenic, although just what compound he used I do not know, but

presumably it was salvarsan, although he does not mention this drug after using it in recurrent fever.

Frambœsia.—In 1910 Nichols succeeded in inoculating a rabbit's testicle with material taken from the lesions of frambœsia. The resulting lesions very closely resembled those of rabbit syphilis and were cured by salvarsan. At that time it was already known that atoxyl would cure frambœsia. The cure of relapsing fever by salvarsan was also reported from Cairo, Egypt. Since it was known that trypanosome disease could be made to yield to these new arsenicals, the term "therapia sterilisans magna" as applied to salvarsan did not especially apply to syphilis alone but to the entire series of trypanosomic diseases. In this connection it is interesting to note that Ehrlich brought out the curious fact that in some parts of Africa the response of these diseases to the new arsenicals was more satisfactory than in others. This was particularly so in sleeping sickness. Ehrlich also discovered that it is possible to immunize rats against trypanosomiasis.

We will now discuss in more detail the most important of the trypanosome and spirillose diseases, which from their cause and clinical course, are analogous to syphilis.

Sleeping Sickness.—Of these, the best known is sleeping sickness, so-called because of the lethargy and somnolence which is characteristic of its second stage. This disease has been known for more than five hundred years, but its cause was not discovered until Dutton described it in 1901; although Forde had previously called attention to a parasite found in the blood plasma of those suffering with the disease.

The organism is a small fish-shaped flagellate, actively motile, which multiplies by fission in its long axis. It is about three times the length of a red blood corpuscle. It is provided with two nuclei. The principal nucleus is in the middle and a smaller one at the blunt end. A long thread-like process runs the entire length of the body and goes to form the undulating membrane, and passes beyond the sharp end of the body as a free flagellum. Resistant forms and resting forms have been noted. These are small round bodies with two nuclei but lacking the flagellum. They are also infectious. Experimental chemotherapy indicates that several types exist.

Man is infected by the bite of the tsetse flies—*Glossina palpalis* and *Glossina morsitans*. The first of these is found on the banks of streams, and in marshes and lowlands; the other in higher altitudes.

The trypanosomes when ingested by the fly undergo a cycle of development in the digestive tract. Sexual forms appear and their numbers increase. In about three days they become infec-

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tive and this infectivity continues for about two and a half months. It is probable, however, that the fly once infected remains so for life; that is, for a year or more. Only about 5 per cent of the flies ingesting the organism are infective to man. Koch and Kudicke were of the opinion that the disease could be transmitted by sexual contact. Laveran and Mesmil state that trypanosomes produce specific agglutinins, precipitins and trypanolysins which enable a differentiation of morphological varieties to be made. Some of these trypanosomes are peculiar to animals, causing the diseases known as surra, dourine and nagana. The sleeping sickness in different parts of Africa as Rhodesia and Nyassa arises from different trypanosomic species. The Rhodesian type is extremely virulent.

Sleeping sickness has an incubation period of from ten to twenty days. The onset of the disease is gradual and insidious. There are fever, chills, headache and vomiting, not unlike a mild attack of malaria. The trypanosomes may be present in the blood at this stage. Following this febrile attack the patient feels well for several days or even for as long as several weeks. Then comes a second febrile attack. These attacks of fever alternating with periods of normal temperature may go on for months—the so-called trypanosome fever. A distinctive feature during this phase of the disease is a hyperesthesia of the deep muscles on pressure. As the disease progresses the patient has headache and pains in the legs and arms and a painless cervical adenitis develops. In white men there are fleeting erythemas. Edema of the ankles and face is a symptom not infrequently present. The anemia becomes severe. The leukocyte count remains low but there is a relative increase in the large and small mononuclear cells. The recurrent febrile attacks naturally suggest malaria or relapsing fever. The exanthem and adenitis suggest early secondary syphilis. There is swelling of the spleen. Puncture of the lymph nodes reveals the presence of the parasites which are also present in the blood during the periods of pyrexia. The exanthem consists of a papular eruption with sometimes an independent outbreak of an annular erythema. This annular appearance suggests the circinate character of many syphilitic cutaneous lesions.

After these febrile attacks have lasted for a number of months the symptoms from whence the disease derives its name—"sleeping sickness"—develops. This is due to the invasion of the central nervous system by the parasites. The patient becomes depressed and apathetic; he is unable to concentrate his mind. He becomes mentally defective. Epileptiform attacks may occur. Gradually these symptoms become more pronounced. The lethargy and somnolence become more profound. The patient sleeps all the

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time, even having to be roused to eat. There is rapid emaciation, decubitus, and death occurs from a terminal sepsis.

The disease may last for years, but once the nervous system is involved it is invariably fatal. A peculiar feature of the spinal fluid is the enormous increase in the number of lymphocytes. The globulin increase is also pronounced.

Chagas's Disease.—The South American form of trypanosomiasis is known as Chagas's disease or thyroiditis parasitaria. This affection is due to the Schizotrypanum cruzi and is introduced into the body by the bite of an insect. It is endemic in Brazil, occurring among children. It may be either acute or chronic. The acute form attacks infants under one year. There is a general adenopathy which is most pronounced in the neck. There is periodic fever and a marked tendency to edema. The nervous system may not be implicated, but there is a nervous form of the disease which is characterized by spastic paralysis and athetosis. The spleen and liver are enlarged. The trypanosomes can be found in the blood from ten to twenty days after the onset of the disease. The muscles particularly are attacked by reason of the fact that the parasite lives on the muscle plasma. Accompanying the symptoms already mentioned, the thyroid becomes enlarged and this is followed by symptoms of myxedema such as dry and scurvy skin and bradycardia. If the patient recovers there is usually some permanent injury to the nervous system remaining.

The parallelism between this disease and syphilis is readily apparent. I need only call the reader's attention to the lymphatic enlargement and the predilection of the trypanosome for the nervous system.

Relapsing Fever.—The analogy of syphilis to relapsing fevers is not at first apparent. The disease is caused by a flagellate spirocheta discovered by Obermeier in 1868. The parasite is corkscrew shaped and about 10 to 40 μ in length. The relapsing fever of different parts of the world is caused by different varieties of the same parasite, the European form being known as the Spirochæta obermeieri, the African as Spirochæta duttoni, the American as Spirochæta novyi, the Asiatic as Spirochæta carteri.

Human beings are infected by the bites of lice and ticks. The disease has numerous synonyms, which simply shows that the clinical manifestations are the same irrespective of the part of the world in which the disease occurs. It is ushered in with fever, chills, headache, backache, tinnitus and pains in the extremities. In some cases these are accompanied with constipation, vomiting and splenic enlargement. The blood picture shows only moderate leukocytosis with a slight increase of the polymorphonuclear elements. The fever lasts about a week and then falls by crisis.

An interval of five or six days, or at times, of more than two weeks, then elapses before the second attack, which is usually a day less in length. The majority of cases end with this second attack, but in about 7 per cent there is a third and even a fourth attack, these last two attacks being much shorter than the two previous. Occasionally during the afebrile period following the first attack an intense jaundice sets in. This is due to a pyogenic sepsis. The mortality of the disease varies from 2 to 10 per cent.

The symptoms other than the fever can be attributed to the bacteriemia and resemble those of the acute infections rather than syphilis. There are no distinctive anatomical findings on post mortem except those seen in acute blood states generally. These, of course, would include visceral degenerations. That it yields to arsphenamine and other arsenicals and its occurrence in a series of relapses with free intervals between are the principal features it shares in common with syphilis. Muco-cutaneous Leishmaniasis, or to use its common name, Espundia, also Uta, Bubas Braziliana, Smith's disease, Breda's disease, is a destructive affection which in certain respects resembles syphilis. The cause of this disease is a protozoön, Leishmania brasiliensis, which is the American variety of Leishmania tropica. It is an extremely chronic ulcero-granulomatous affection of the skin and mucous membranes of the mouth and nose. It is a most ancient disease as it was known to the Incas long before the discovery of America. It is barely possible that this disease may have been confused with syphilis by the early Spanish observers.

The period of incubation is unknown. It begins with a nodule which quickly breaks down and forms an ulcer. This initial lesion has been called by Escomel "espundial chancre." The ulcer is very chronic, lasting for many months or even years, but eventually it heals leaving a scar. While the primary sore is still active but usually after it has healed, the characteristic ulcerous granulations appear on the mucous membranes of the mouth and nose and also at times on the cutaneous surface of other parts of the body. The disease attacks the hard and soft palate, also the gums and lips. The nasal cartilage is frequently destroyed, causing considerable deformity. Strange to say, however, the underlying bones are rarely attacked. The ulcerative process may extend to the pharynx and larynx, causing aphonia and dysphagia. The disease is characterized by extreme chronicity. It may last for twenty or thirty years. A profound cachexia may supervene and the patient may die therefrom, but usually death is caused by some intercurrent disease. Occasionally the vaginal mucous membrane is affected instead of that of the nasal and buccal cavities.

Although a protozoal disease, espundia does not respond to

organic arsenic or mercury and this is one of the means whereby it can be diagnosed from syphilis. Tartar emetic or antimonii et potassii tartras is specific to it and since antimony belongs to the same group chemically as arsenic the therapeutic difference is not as marked as it would otherwise seem.

Kala-azar.—Kala-azar—the black or mortal sickness, or tropical splenomegaly, also called Dumdum fever, is a tropical disease, the most marked features of which are enlargement of the liver and spleen, an increasing anemia, accompanied with a decided cachexia. The disease is common in India and throughout the East. It was formerly supposed to be a form of malaria, but in 1903 Ross discovered the parasite Leishmania donovani in the cells of the spleen. The disease is probably transmitted by an insect, the Clinocoris rotundatus or the Conorrhinus rubrofasciatus.

There is an incubation period of about three weeks, which, however, may be longer. Leishman divides the disease into three stages: an initial stage, a febrile stage with splenomegaly and a cachetic stage. The disease is characterized by irregular fever—two elevations every twenty-four hours, a progressive anemia and an extraordinary leukopenia—the white blood cells sometimes sinking as low as 1000. Kala-azar is a chronic disease, its usual length being from six months to a year and a half. It may, however, last only three months or it may be prolonged for a decade. Its mortality is very high: nearly 100 per cent without treatment and 70 per cent with treatment. The parasites can be demonstrated in the leukocytes in blood smears, but diagnosis in this manner is often difficult. It is much easier to diagnose their presence in the juice of the spleen, although puncture of that organ is not unattended with danger from hemorrhage. For that reason the liver is usually the organ selected. The parasites may also be found in the bone marrow, and for diagnostic purposes resection of a rib or trephining the tibia is sometimes resorted to. Since the parasites also occur in ulcers of the intestines their presence is sometimes demonstrated in the feces.

Mediterranean Kala-azar.—Mediterranean kala-azar, or infantile leishmaniasis, is prevalent on the shores of the Mediterranean Sea. It is caused by the Leishmania infantum. It is essentially an infantile disease. The pathology of the disease has been studied by Pianese. The liver and spleen are much enlarged, especially the spleen. There is also hypertrophy of the islands of Langerhans in the pancreas and changes in the bone-marrow.

The disease begins insidiously, usually with some disturbance of the alimentary canal. The appetite, however, remains normal and may even be increased. The symptoms are enormous enlargement of the spleen, marasmus and diarrhea. The diarrhea may

alternate with constipation. The anemia is not so marked as in adults but, as in adults, there is also leukopenia. It is extremely difficult to discover the parasites in blood smears in the infantile form of the disease. The malady is transmitted by fleas. Small animals are susceptible to the disease experimentally.

Oriental Sore.—The form of leishmaniasis, which very closely resembles syphilis, is cutaneous leishmaniasis or oriental sore, also called Delhi boil, Aleppo boil, and many other names too numerous to mention, not however because it is confined to the Orient, for it also exists in a severe form in Brazil, Peru and Paraguay, where it is variously known as Pian-bois, or forest yaws. While not so severe a constitutional disease as the preceding types of leishmaniasis yet it is a destructive affection which bears a certain resemblance to syphilis. It can be experimentally induced in dogs and monkeys, as has been proven by Nicolle and Marceaux. The initial lesion, known as the chancre, begins on some exposed part of the body, usually during the summer or autumn, and is undoubtedly caused by the bites of insects. Ulcers form which may cause extensive destruction of the part attacked. After healing these give rise to cicatricial deformities. The disease yields promptly to the internal and external use of antimony which is closely related to arsenic chemically. The latter, strange to say, is inert in this case, as it is in espundia to which it bears a rather close resemblance.

Weil's Disease.—Spirochetosis icterohæmorrhagica, also known as Weil's disease, epidemic jaundice, infective jaundice, is a spirochetal disease that seems to differ from other spirochetal and protozoal diseases in many important details. The disease is relatively common in the southern part of the United States. It is resistant to arsenic, quinine and other spirillocides and trypanocides. It is, however, amenable to serotherapy and for this and other reasons resembles a bacillary disease. Indeed, until Japanese observers proved otherwise, it was supposed to be due to the Bacillus proteus vulgaris or the Bacillus paratyphosus. It is not definitely known whether it can be transmitted by insects or not. The causative organism, the Spirochaudinnia icterohæmorrhagica, is parasitic to rats. The jaundice is probably caused, according to Castellani, by an obstruction of the minute bile ducts brought about by a polymorphonuclear exudate into the tissues surrounding them. There is no relapsing feature in the disease except in some instances there is a single relapse such as not infrequently occurs in all infectious maladies. Because of this fact it would seem that in this affection at least the assertion that the spirochetes necessarily cause infections of a single type does not always hold. The incidence of the malady is also peculiar. It is a disease that occurs often in armies, although it is not to be confused with "camp jaundice"—

Icterus castrensis levis. As already stated, it is also relatively common in the southern part of the United States. The disease has shown a tendency to appear in other countries during wars and there is evidence of its great antiquity. It is also apt to become prevalent in prisons and wherever many people are gathered together in unsanitary surroundings. It is not endemic over large parts of the earth's surface as is syphilis. The spirochete causing the malady is said to be able to pass through the unbroken skin. Since it is known that the organisms pass out through the urinary tract it can be assumed that the soil is thereby infected. Unlike most other spirochetal diseases, there is no primary lesion or local reaction. The disease attacks butchers and cooks more frequently than others. This fact is difficult to explain, or rather, it is open to a number of explanations. Workers in sewers and drains are also attacked, as is natural to suppose. Clinically it presents no symptoms resembling syphilis. The onset is sudden with high fever and much prostration. There is jaundice, which may be slight or severe; there is enlargement of the spleen and albuminuria. After about a week or more the fever slowly falls and the symptoms abate. In some cases, as already stated, there is a mild relapse after about a week. As would be inferred by the jaundice, there is a tendency to hemorrhages of various kinds. A form resembling Weil's disease is endemic in Japan, where it is known as Nanukayami. It is also caused by a spirochete—Spirochæta hebdomadis.

Rat-bite Fever.—A disease somewhat common in Japan, but less rarely seen elsewhere, is sodoku or rat-bite fever. It is caused by Spiroschaudinnia morsusmuris. The period of incubation is from one to two weeks. There is a characteristic local reaction represented by redness about the bite and swelling following which an ulcer appears with regional adenopathy. This slight sign of infection soon subsides and the first evidence of a generalized infection is an arthralgia involving all or nearly all the joints. This is followed almost immediately by a maculo-papular eruption accompanied with lassitude and anorexia. The eruption is mostly on the extremities and is not attended with itching. It quickly disappears leaving no trace. During the eruption there is fever. There are periods of remission during which time the patient is free from symptoms. Each exacerbation is attended with an eruption. There is always a severe anemia which may be very protracted. During the eruptive period one or more of the joints may also react. A distinctive analogy of the disease to syphilis is that it readily yields to arsphenamine.

Gangosa.—A disease thought by some to be either a special form of syphilis or yaws is gangosa, a word which means nasal voice.

It is a destructive ulceration of the palate and nasal passages and cutaneous surfaces. It occurs only in isolated localities in Polynesia and Australasia. It is prevalent in Guam. Those who have studied the disease are convinced, however, that it is neither syphilis nor yaws, although it very closely resembles the tertiary lesions of both. Neither can it be identified with leprosy, tuberculosis or blastomycosis. Cases said to have been gangosa which were observed in the West Indies and at Panama, were later proven to have been some one of these diseases and not gangosa. A peculiarity of the disease is that it confines its attacks only to negroes and Malays. It is conjectured that the disease, while neither syphilis nor yaws, yet is closely allied clinically to both although its causative organism is unknown. It is believed that the lesions are contagious and are the means of transmitting the disease.

The disease begins with an ulceration of the palate. The ulcerative process spreads upward with great rapidity, destroying in its course the bones and cartilage of the nose. Not infrequently the nasal ducts are involved with consequent loss of one or both eyes. The length of the disease is about one or two years when the ulcerations heal leaving oft times hideous deformities. Ozena is a frequent concomitant of the disease. In spite of its chronicity and the cruel mutilations, to which it gives rise during the course of the disease, the general health is not affected.

When Numa Rat investigated yaws in the West Indies, in 1891, he described many cases which would seem to be undistinguishable from gangosa but it is now believed that they were cases of tertiary yaws.

Recently Leys, who has investigated the subject most thoroughly, has demonstrated beyond a doubt that the gangosa of Guam is a distinct disease and while akin to syphilis and yaws does not depend as a cause upon either Treponema pallidum or the Treponema pertenue. Leys also asserts that the disease is endemic to the Island of Dominica in the West Indies. It is not amenable to mercury but responds somewhat to arsphenamine.

Ulcerating Granuloma.—A chronic ulceration of the genitals endemic to tropical countries is ulcerating granuloma. The cause of the disease has not, at the present writing, been ascertained, although Wise, who has studied the disease, is of the opinion that it is due to a spirochete resembling the Treponema pallidum. Many bacteriologists however, are of the opinion that it is caused by the so-called Donovan bodies which have been found in abundance in the lesions. Walker asserts that it is caused by a capsule bacillus of the *Bacillus mucosus capsulatus*, Friedländer group; while Arago and Vianna consider it of the type species, *C. granulomatis*. Like syphilis and chancroid it is a venereal disease, being transmitted

in most instances by sexual contact. It is said to be more frequent in women than in men. The disease begins as a small, painless papule or nodule on the penis, labia, or the perineum. The lesion soon ulcerates and the ulceration spreads to the groins and the inner surface of the thighs, not unlike phagedenic chancroids such as were formly seen but which are now exceedingly rare. The ulcer has clean-cut edges and its base is covered with a gray membrane somewhat diphtheritic in appearance. There is a profuse and offensive discharge. Granulations are present which bleed easily. The progress of the sore is very chronic and it heals with scar formation. The adjacent lymph glands are not involved. The process is painless and there is no impairment of the general health unless the erea involved is extensive. It responds to tartar emetic therapy but not to organic arsenic or mercury.

Verruga Peruviana.—A tropical disease endemic to isolated valleys in Peru is verruga peruviana. While the specific organism has not as yet been discovered it is undoubtedly an infectious granuloma and, therefore, more or less related to syphilis.

The disease is characterized by a vesicular and papular eruption over the face and extremities. These are followed by subcutaneous nodules which may attain considerable size. Over the nodules the skin breaks down and upon the ulcerating surface thus exposed red fungous growths develop. The eruption lasts for weeks or months and then subsides. Recurrences are common. The nodules have also been found in the internal organs at autopsy. The disease is frequently combined with oroya fever of exceedingly high range, a rapidly developing and pernicious type of anemia, attended with great prostration and usually followed by death. The course of the disease is about a month or six weeks. Barton, and later Strong, have each described a hematazoön, distinct from all others, now known as the cause of the disease. Oroya was formerly considered to be the febrile stage of verruga peruviana, but that it is a separate disease entity has been established by the researches of the expedition to South America of the Harvard School of Tropical Medicine.

The spirochetal disease, which has the closest analogy to syphilis and which is yet by some confounded with lues is yaws or frambœsia.

Frambœsia.—Yaws is essentially a disease of tropical countries where it is more or less endemic. In the United States and Europe it is rarely, if ever, seen except as an importation. In 1905 Castellani demonstrated the presence in skin lesions, lymph nodes and the spleen of a protozoön which he named the Treponema pertenue. Sometime later Neisser and his colleagues showed that the disease could be induced experimentally by inoculating material from human beings into apes. An orang having been inoculated, four

months later developed a general eruption. This fact is of special interest because it is shown in another chapter that syphilis in the orang remains strictly localized. In this experiment the eruption appeared as papules on the chest, abdomen, extremities and face, and were in every way typical of yaws. The eruption underwent spontaneous involution. Following upon this Castellani inoculated 5 inferior simians and in 3 of these obtained similar secondary manifestations. I again desire to call the reader's attention to the fact that these animals do not develop constitutional syphilis when inoculated with the Treponema pallidum. These experiments were repeated by various workers with the same results. The period of incubation, at least in the experimental disease, was established to be twenty-four days—about that of the chancre—and one observer also found the Treponema pertenue in the initial lesion. Material from one of these lesions was then inoculated into a rabbit's testicle and in due time nodules appeared in which were found the Treponema pertenue.

Castellani then succeeded in producing the initial lesion of yaws in the skin of the scrotum of a rabbit by grafting under the integument some material obtained from a testicular nodule supplied by Nichols, an American observer then working in the Philippines. Two nodules resulted from this experiment. Of these, one ulcerated and the resulting sore exactly resembled the corresponding lesion as seen in rabbit syphilis. Castellani then scarified the scrotum of a rabbit and applied some secretion obtained from a yaws lesion. This was on December 20. On January 16, twenty-seven days later there were evidences that an initial lesion was developing. On January 27 the lesion had fully developed and the serum obtained therefrom contained the characteristic treponema.

Castellani's experiments showed that passage through the rabbit added to the virulence of the disease—the chancres thus obtained being better developed and the percentage of positive results being larger. The chancre of yaws in the rabbit shows no points of difference from the same lesion in syphilis, and this applies both to appearance and to the period of incubation. Castellani now proceeded to cause experimentally generalized yaws in rabbits. With this object in view, tissue from the testicle of a rabbit infected with the disease was injected into the vein of another rabbit. The experiment was repeated a number of times. In a way the results were positive. After a variable period of incubation papules appeared on parts at a distance from the point of inoculation. Some of the lesions ulcerated. Other reactions which developed varied in character. Some of the young animals inoculated showed no retardation of growth; others did. The nodules which formed

in the deeper structures of the nose, it was observed, ulcerated and were attended with loss of appetite and symptoms of malnutrition. Castellani likened these lesions to syphilitic gummata, which indeed they most closely resembled.

In the experimental yaws produced in rabbits there has been observed two types of lesions—papules and granulomata. The former affect principally the face of the animal and appear either isolated or in groups. Not infrequently they attain a considerable size and ulcerate. Over the ulceration a yellowish crust forms which, upon being detached, reveals a raspberry-like ulcer. Microscopically these lesions are identical with those observed in human beings suffering with the disease. The granulomatous lesions form gumma-like tumors which have a tendency to appear in the nose and tail. Histologically they are true granulomata.

Castellani asks the question, "Is yaws syphilis?" We have unicists, dualists and those who refuse to commit themselves. Neisser holds that they are quite dissimilar diseases which can occur side by side independently of each other. His opinion has been strengthened by the fact that there have been many instances of the development of the disease in those already affected with syphilis. On the other hand, Levaditi believes that while nominally dissimilar, they are but different forms of the same affection. The two maladies have been termed twin sisters because they are identical in so many ways. On the contrary, however, typical cases of such disease can be readily differentiated. But again, there are many cases of both diseases in which experts in tropical medicine and dermatology have been unable to diagnose between them. This confusion in diagnosis is noted, especially in tertiary lesions. Nor does bacteriology and serology help us much because the two causative organisms cannot always be distinguished, and yaws also gives a positive Wassermann reaction. Both diseases are cured by arsphenamine, which furnishes another analogy. Animal experiment seems to be the only sure test, because the lower simians do not develop constitutional syphilis but do develop constitutional yaws.

To further differentiate between the identity of syphilis and yaws, crossed inoculation experiments have been made. Research along these lines is old; as far back as 1881 Charlouis showed that in man neither disease protected against the other. Many years later, Neisser and Castellani studied crossed inoculations in animals and proved again that neither disease protects against the other. On the other hand, Levaditi was unable to inoculate syphilitic apes with yaws. Nichols cured syphilitic rabbits with arsphenamine and then inoculated them with yaws. The first tests gave positive results, and later when positive results were noted there was evidence of the development of a slight immunity

by reason of which the incubation period was longer and the initial lesions smaller than usual. This slight protection Nichols ascribed to the action of arsphenamine in causing the development of syphilitic antibodies. Crossed inoculation experiments can only be final when it is known that a general infection occurs; if immunity is only local no positive conclusions can be reached.

Nichols states that the eruption—the "yaws"—is always the same. There are no atypical forms and they always present the raspberry lesions. The lesions of yaws are autoinoculable, a fact, I might add in passing, which seems to have received scant attention. In yaws it is noted that the giant cells are absent. This is one of the histological characteristics of syphilis. It also seems to me to be incongruous to divide yaws into primary, secondary and tertiary forms, because the disease does not seem to conform to this arrangement. It is true the disease begins with a primary lesion which may sometimes appear on the genitals. This primary lesion is the "mother yaw" of the old writers. In females the primary lesion may appear on the breast and in children on the feet due to inoculation by an insect. The interval between the primary and consecutive lesions is from one to three months. These constitutional symptoms being much less clear and characteristic than those occurring in syphilis, and for that reason, as I have just stated, it does not seem advisable to divde the disease into arbitrary stages as some would do. The outbreak is general and is distinctly not due to autoinoculation. The extremities, face and chest are most frequently attacked, and, as is also the case in syphilis, there are apt to be papules about the anus.

Castellani, who I may say is our highest authority, is decidedly of the opinion that tertiary yaws is a reality. It may be delayed for many years. It shows as a gummatous process which, like its congener, syphilis, may attack almost any of the tissues of the body. As in syphilis, secondary and tertiary lesions may exist side by side. Unlike syphilis, however, yaws shows no predilection for the nervous system or the circulatory system.

The initial lesion appears as a small papule. This ulcerates, showing a yellowish-red base from which a seropurulent fluid exudes. The sore assumes a fungus-like growth and may attain a diameter of one or two inches. In from six weeks to three months a generalized papular eruption appears. The face, neck, perineum and extremities are affected. It is frequently attended with itching. This is in sharp contradistinction to syphilis in which the lesions rarely, if ever, itch. There is also a uniformity in the lesions which is not the case with syphilis. The onset of the eruption is usually attended with fever, headache and arthralgia. The eruption usually lasts about three or four months, but it may be pro-

longed for several years by successive eruptions. In a few cases tertiary lesions in the form of gummatous nodules and ulcerations appear. Recovery nearly always occurs but reinfection can take place. There is always a positive Wassermann. Arsenicals act upon yaws even better than upon syphilis. Gangosa, which I have already mentioned, is thought by some to be a tertiary form of yaws. This view I do not hold, but believe it to be a separate disease entity. An important clinical distinction between syphilis, yaws and gangosa is that the two last-mentioned diseases frequently attack children. The fact enables us to remove them from the list of venereal diseases *per se* and place them in the same category as syphilis insontium.

There have been at least two series of experimental human inoculations of yaws. In 1848 Paulet inoculated 14 healthy persons with yaws and the initial lesion appeared in from twelve to twenty days. In 1881 Charlouis inoculated 28 individuals, with an average incubation period of fourteen days. However, when the disease is transmitted in the usual manner, the period of incubation is known to vary extremely, in some instances the period of incubation being prolonged to six months. The primary and secondary papules of yaws appear to be more superficial than those of syphilis, the deeper cutaneous layers not being affected. Many cases of so-called "frambœsiform" syphilides indicate that the Treponema pallidum can also produce similar superficial lesions. The general tendency of the disease to spare the mucosa explains the absence of ordinary contact infection as is seen in syphilis. An infant with yaws does not infect its nurse and a woman with the disease does not have the moist papules of the vulva so frequently seen in syphilis.

Analogy of the Trypanosome Diseases.—In concluding this chapter, I desire to call the reader's attention to the fact previously exemplified in Spielmeyer's masterly monograph concerning the analogy of the trypanosome diseases to each other, not only from the histological standpoint, where the resemblance is very close, but also from the clinical point of view as well. In sleeping sickness, for instance, there is somnolence, delirium and diminished intelligence. Later there is ptosis, tremor, speech disturbances and convulsions. In dourine we see focal nerve lesions, such as anesthesia, ataxia and paraplegia. Now if we combine the phenomena of several of these trypanosome diseases—such as dourine and sleeping sickness—into a theoretical affection as it were, we at once observe a striking number of phenomena common to the two groups. First is the fact that the disease is frequently transmitted by coitus, the initial lesion appearing upon the genitals in from two or more weeks. This initial lesion is followed by adenopathy and a generalized eruption. There may also be alopecia and keratitis. If we pass

from these manifestations to cerebral syphilis we see in the cerebral symptoms of sleeping sickness and in the histologic changes in the cerebral cortex a very marked parallelism. If now we pass to the sleeping sickness artificially induced in the dog we see the analogy to human tabes. In conclusion, we see all of these diseases favorably influenced by the various forms of organic arsenic.

From the facts as I have studied them and as they have been studied by others, I am of the opinion that this similarity in symptomatology as well as pathology is due to the more or less close resemblance of all spirochetes and trypanosomes, and in the life cycle of the same. Undoubtedly as these analogous diseases are further studied our knowledge of syphilis will be correspondingly increased.

CHAPTER V.

THE PATHOLOGY OF SYPHILIS.

Syphilis is a chronic, infectious and contagious disease, partaking of the character of a specific fever and an infective granuloma, the cause of which is the Treponema pallidum.

Incubation Period.—After exposure to infection there is a period of incubation which may be as short as ten days or as long as sixty; usually it is about twenty-one days. During this time there are no symptoms whatsoever, nevertheless the infective agent—the Treponema pallidum—is actively propagating in the body.

The Chancre.—The earliest of the phenomena of the syphilitic toxemia is the initial lesion or chancre; the appearance of which constitutes the so-called primary stage of syphilis. The delay in the development of the chancre is due to the fact that, in accommodating themselves to the host, many of the organisms are destroyed by the tissue-protecting forces, in consequence the chancre does not appear until they have increased sufficiently to produce the lesion. At the beginning the chancre is an inflammatory process superficially seated at the point of entry of the infection. Within a few days the inflammation extends downward into the subcutaneous or submucous layers of the surface upon which it appears. Within its area, which is small, and in the tissues immediately around it, the lymph vessels are dilated and filled with leukocytes. There is also an obliterative endarteritis. Simultaneously with this there is a small-cell infiltration of the connective tissue and a proliferation of the connective-tissue cells. Epithelioid cells and a less number of giant cells are also found. When these changes are complete the height of the process is reached and the center of the neoplasm, owing to the obliteration of its blood supply, disintegrates by ulceration. A thin crust, or pellicle, forms over the ulcerating surface, which, to the experienced eye, is distinctively characteristic. After about ten days the lesion begins to resolve at its periphery; this occurs by a fibrous consolidation of the new growth. It then assumes the cartilaginous hardness by which the chancre is pathognomonically distinguished. In a month or six weeks the lesion heals, leaving only a slight scar, the destructive ulceration having been expended upon the proliferated tissue. For some time thereafter, however, a nodule may be felt beneath the surface; and this may not disappear for several months.

Lymphatic Involvement.—Concomitant with the appearance of the chancre there is an enlargement of the lymph nodes of the lymphatic system of the locality wherein the chancre is situated. As in the chancre there is an infiltration of small cells and a proliferation of connective-tissue cells. This glandular enlargement is discrete—not matted as in tuberculosis; it is not attended with pain, and suppuration does not occur unless pyogenic organisms are also present. The glandular involvement, which is at first local, in the course of a few weeks becomes generalized so that glands far removed from the lesion have the characteristic "shotty feel" of those in the immediate vicinity of the chancre.

From six weeks to six months is the so-called period of secondary incubation. During that time there may be no symptoms at all except the gradually extending glandular enlargement.

Secondary Symptoms.—At the end of that time the secondary symptoms appear. Rarely in untreated, and quite frequently in cases that have been vigorously treated as soon as the chancre has been diagnosed, these secondary symptoms fail to appear. As a rule the secondary symptoms take the form of an eruption but this eruption may be preceded by fever, headache, bone pains and general malaise. The eruption may consist of macules or papules, or it may be vesicular or pustular. With the development of the eruption there appears on the mucous and muco-cutaneous surfaces an exudative and productive inflammation of the papillary layers which goes on to ulceration and consequent exfoliation of the epithelium. The lesions so produced are known as mucous patches and are especially characteristic of secondary syphilis. The lesions of secondary syphilis are in the nature of metastases and represent the reaction of the tissues to aggregations of the Treponema pallidum in some particular spot—either on the skin in the form of a roseola or widely disseminated papules, or on a mucous surface as an erosion or mucous patch, or in the eye as an iritis. The lesions of the secondary stage preserve a certain general order in their evolution and they are more or less transitory. Further, in the secondary stage the lesions may be widely present and yet the general health may be only slightly or not at all affected.

Blood Picture.—The blood picture in secondary syphilis is not characteristic. There is frequently a decided fall in the hemoglobin percentage, which may fall as low as 75 per cent. There may also be a fall in the number of red blood cells. This anemia, if present, reaches its height when the eruption is fully developed and disappears after the eruption fades. A moderate leukocytosis is present in the secondary stage, but this leukocytosis is not due to polymorphonuclear leukocytes as it would be in an ordinary septic infection. The most abundant cells are the lymphocytes, and there

is an eosinophilia which is in proportion to the intensity of the cutaneous eruption.

Mucous Patch.—Of equal frequency with the skin eruption in the secondary stage is the erosion or mucous patch as it is generally known which is found usually in the mouth, and in the vagina in females. These lesions, occurring in the esophagus or stomach, are practically unknown. The same is true of the intestines. The spleen and likewise the liver may be enlarged in early secondary syphilis—the liver very frequently. The enlargement of these organs is an engorgement rather than a connective-tissue hyperplasia and soon disappears. Jaundice, occuring in secondary syphilis, is not uncommon and is probably due to this engorgement narrowing the lumen of the ductus communis choledochus or to irritative changes in the liver cells.

An erythema is sometimes seen in the nasal passages and these spots may ulcerate and give rise to the epistaxis occasionally observed in secondary syphilis. The same may occur in the larynx. There are no changes, so far as is known in the secondary stage referable to the trachea, bronchi or lungs.

The heart and vessels are not affected in secondary syphilis, although it has been asserted that endocarditis may occur. The bones and joints are not affected in the secondary stage except an occasional periostitis of one or more of the long or flat bones and a transitory arthritis—the so-called syphilitic rheumatism.

Nervous Lesions.—I am in accord with MacCallum that the lesions of the nervous system are essentially of the tertiary stage in so far as pathology is concerned, although in point of time they not infrequently occur within the cycle assigned to the secondary stage. I believe, however, that meningitis may occur as a purely secondary lesion. While secondary syphilis produces no grave changes in the nervous system, there is no doubt that it is during this stage that the Treponema pallidum invades the nervous system and gives rise to the profoundly enervating changes in the brain and spinal cord which are characteristic of tertiary syphilis.

Three Stages.—It was the French syphilologist Philippe Ricord who suggested the division of the disease into three stages, and although eighty years have passed this division is still pathologically sound. This division, however, is purely arbitrary. In the evolution of syphilis these stages are not always sharply defined and separated from each other. For, the chancre may be still unhealed when the secondary stage is ushered in by a roseolous eruption. Thus, the first and second stages may be said to overlap. Again, tertiary lesions, that is, gummata, may appear precociously, and the patient pass from the first into the tertiary stage, skipping the second stage. Or, tertiary lesions may be present in proximity to

secondary lesions. It is also possible for a secondary lesion to appear many years after the primary lesion, when, in point of time, the lesion should be considered tertiary. There may be no secondary stage, the tertiary stage not showing for many years after the primary stage. The tertiary stage may never appear.

Tertiary Stage.—In the tertiary stage of syphilis the deeper organs and tissues are attacked. The lesions of the tertiary stage, unlike those of the secondary, are destructive and frequently threaten the patient's life. It is the stage when syphilitic visceropathies occur. It must be understood, however, that the tertiary stage is not an inevitable phase in the evolution of the disease. The majority of syphilitics never enter this stage. It has been estimated that approximately 15 per cent of all those infected with syphilis develop tertiary symptoms. It is held among syphilologists generally that adequate treatment can prevent them. This does not always hold good however, especially in regard to the nervous system. Between the secondary and tertiary stages there is almost invariably a period of latency, during which time manifestations of the disease are absent. This period of latency, when the treponemata are dormant, was first noted by Virchow and is still one of the unexplained mysteries of syphilis. During this latent period the patient may enjoy perfect health and display absolutely no signs of the disease except a positive Wassermann reaction in the blood or spinal fluid. This asymptomatic stage usually lasts about two years, although it may be extended to thirty or forty years, or even longer.

The Gumma.—The characteristic lesion of the tertiary stage is the gumma. In addition to this, pathologists of the present day also recognize an equal tendency to the proliferation of granular cellular tissue which later becomes fibrotic.

A gumma is a nodular neoplasm from which no tissue is exempt. It may vary in size from a millet seed to an orange. Gummata are composed of small spheroidal and epithelioid cells in the center with a periphery of wandering cells. Histologically the gumma is almost identical with the tubercle. The smaller gummata do not necrose in their center, but sooner or later, in those of larger size, the center breaks down into a necrotic mass of gummy consistency, not unlike thick syrup, hence the name. This central necrotic portion is usually absorbed, and the surrounding aggregation of cells is transformed into cicatricial tissue which may produce a more or less distorting scar.

The cellular proliferation, which later becomes fibrotic and which is also characteristic of tertiary syphilis, is particularly noted in the walls of the bloodvessels and in the supporting connective-tissue framework of the various viscera. The progress of this proliferation toward ultimate fibrosis and consequent impairment or destruction of the part is slow, and may be present without any

subjective or objective symptoms arising therefrom for a long time. Thus are produced the degenerative visceropathies with which every syphilologist is familiar.

Bloodvessels.—The Treponema pallidum has an undoubted predilection for the walls of the bloodvessels. The arteries especially are singled out. All three of the coats are attacked as well as the vasa vasorum. So intense may this inflammation be that the vasa vasorum and the smaller arteries may be obliterated and persist only as minute fibrous cords. Usually the cellular infiltration is evenly distributed but frequently it occurs in circumscribed areas which are true gummata of the vessel walls. In time this cellular infiltration undergoes fibrosis, causing a thickening of the walls in some places and a thinning in others. These fibrous bands are found mostly in the media, while on the intima there is deposited a layer of hyaline fibrous tissue. In large vessels such as the aorta these changes can be seen by the naked eye as longitudinal corrugations or rugæ on the circulatory surface causing the formation of sacculations and dilatations or aneurysms. When these changes occur in the vascular system of the brain there is also more or less involvement of the meninges, and from these arise the psychic and motor disturbances of cerebral syphilis. Syphilis attacks the pericardium, the myocardium and the endocardium. As elsewhere there may be gummata or an infiltration which later becomes fibrotic, causing myocarditis. Gummata are usually found near to or involving the bundle of His.

Lip.—When the lip is involved in tertiary syphilis it is usually in the form of a diffuse infiltration which involves the entire lip. Should the process go to ulceration there may be considerable deformity. This is exactly contrary to chancre of the lip which may be very large and yet heal with scarcely a sign of its former presence.

Tongue.—On the tongue tertiary syphilis manifests itself most frequently as a diffuse infiltration. When a gumma occurs it is usually single. It begins as a circumscribed nodule which later may ulcerate and leave a deep ulcer which has to be differentiated from epithelioma or tuberculosis. The diffuse infiltration, unless absorbed by treatment, sooner or later undergoes fibrosis and the tongue is much reduced in size. The patchy denudation of the epithelium covering the lingual papillæ (known as leukoplakia lingualis) is also of syphilitic origin in the majority of instances.

Esophagus and Stomach.—Gummatous lesions of the esophagus and stomach may occur. Subsequent cicatrization may lead to stricture or to the gastric malformation known as "hour-glass stomach."

Intestines.—In the intestines gummata occur usually in the jejunum or upper ileum. They appear as flat elevations, involving

the mucosa and submucosa. They sometimes coalesce and form an annular ring which, when cicatrization takes place, may cause a constriction. The rectum is the most frequent site of gumma of the alimentary tract. Gummata may form in the submucous coat, usually just below O'Beirne's sphincter, and may ulcerate; or a perirectal gummatous infiltration may form and later give rise to stricture. Gummatous disease of the rectum is more frequent in women than in men and is frequently accompanied with amyloid degeneration of some of the abdominal viscera.

Liver and Pancreas.—The liver is frequently attacked by gummata. They may be widely disseminated of the miliary type, or there may be one or more which may attain a very large size. These large gummata are frequently mistaken for malignant growths. Gummata of the liver may heal with scar formation which may distort the organ by the fibrous bands formed thereby, or there may be a diffuse infiltration which, when it undergoes fibrous change, may give rise to a cirrhosis similar to that caused by alcohol. Where there has been much destruction of the hepatic cells there is usually a compensatory hypertrophy. The pancreas is not infrequently attacked by gummata or gummatous infiltration which in course of time becomes fibrous. Syphilitic lesions of the liver and pancreas, when superficial, may also involve the peritoneum and cause adhesions to form similar to those that sometimes follow an abdominal operation.

Respiratory Tract.—Tertiary syphilis not infrequently attacks the nasal passages, including the bones and cartilages, The gummatous process usually arises in the lining mucous membrane and extends inward to the bone or cartilage beneath. Much destruction and deformity may be caused thereby. Gummata may occur in the hard or soft palate and rapidly ulcerate through so that the nasal and buccal cavities may communicate. The larynx and pharynx may also be affected by gummatous infiltration or a single gumma may attack either one or both of these parts. Tertiary syphilis of the trachea and bronchi is usually of the diffuse infiltrative type which by fibrotic condensation causes stenosis as an end-result. The lungs are affected by tertiary syphilis more frequently, in my opinion, than is usually supposed. Gummata may occur either single or multiple. They are usually found at the base or in the center. They may go on to cavity formation, as in tuberculosis. Should the inflammation be diffuse, fibrosis naturally follows which may closely simulate fibroid phthisis pulmonalis.

Genito-urinary Tract.—Gummata and gummatous infiltrations not infrequently attack the genito-urinary apparatus. Gummata of the kidneys, both large and of the miliary type, have been found at necropsy. There are no symptoms significant of them during life. Should there be a cellular infiltration, sclerosis of the kidneys

will follow, which is similar to contracted kidneys due to some other cause. Gumma may occur in the bladder, also in the prostate and seminal vesicles. Our knowledge of these conditions is comparatively scant, although Thompson has collected a considerable number of references in the literature.

Gummatous infiltration of the spermatic cord has been known to occur. It is very rare. The testicle, however, is attacked by tertiary syphilis with comparative frequency. A gumma may arise in the interstitial tissue and reach an enormous size. In nearly every instance it ulcerates and forms the so-called fungus of the testicle. While there is more or less hyaline degeneration of the tubules, they suffer less injury than might be supposed, so that the prognosis of gumma of the testicle (in so far as restoring the function of the gland is concerned) is not altogether bad. Fibrous changes, however, will render the gland useless. Gumma not infrequently appears on the penis, usually at the site of the primary sore; this is known as chancre redux.

In the uterus and its appendages tertiary syphilis, while rare, is not unknown. It usually occurs as a gummatous infiltration, although gumma of the cervix has been mistaken for carcinoma. Menorrhagia and metrorrhagia may be caused by gummatous infiltration of the endometrium. The same process may attack the tubes and ovaries and the sclerosis following gives rise to sterility more frequently than is usually supposed.

Tertiary Lesions of Bones.—Tertiary lesions of the bones usually affects those superficially located, such as those of the cranium, the clavicle, sternum and the tibia—"the bone that syphilis loves." The pathologic process may originate in the periosteum or in the interior of the bone, that is the bone substance or the marrow. Gummatous infiltration of the periosteum may gradually organize into spongy bone tissue which may continue and finally condense into an eburnated exostosis. Thus are formed the exostoses sometimes seen as "bosses" on the frontal bone, or the peculiar curvature to the shaft of the tibiæ, the so-called "sabre shins" which are pathognomonic of a formerly active syphilis of the bones. The periosteum may separate from the bone and the inflammatory process may continue and involve the cutaneous surface forming an ulcer through which pyogenic organisms will be introduced, causing necrosis of the bone immediately beneath, which will in time be exfoliated as a sequestrum. The cancellous portion of the bone may be attacked first and the cellular infiltration by condensation may thus render the bone thicker and denser. A gumma may arise in the periosteum or in the bone substance. Unless checked by treatment it will invariably cause destruction of the part of the bone involved. Gummata are frequently found in the bone-marrow. If multiple, as they often are, they may

destroy the bone. If they remain stationary they may only be recognized at necropsy; if they extend upward through the cortex and periosteum they may ulcerate or else impart a characteristic spindle shape if it is one of the long bones that is involved.

The joints, tendons, tendon sheaths and bursæ are sometimes attacked by gummatous infiltration. In a joint this may be primary or it may be from extension from the articular surface of one or both bones. As in all tertiary processes the tendency is to end in fibrosis, and the consequent contracture may cause ankylosis.

Nervous System.—That the Treponema pallidum exerts what may almost be termed a selective action on the nervous system has been known practically from the time the organism was discovered. Long before that time, however, pathologists and clinicians were united in the opinion that many nervous lesions were the more or less remote results of syphilis. Some of these lesions they designated as parasyphilitic or metasyphilitic, according to the acceptance of the terminology of Fournier or Mœbius. Modern investigators, particularly Leishman and Noguchi, have shown that they are definitely syphilitic inasmuch as they are due to the presence of the Treponema pallidum in the nervous tissue and its supporting connective tissue.

The cord is more frequently affected than the brain. Both may be the seat of gummata but, contrary to the usually accepted opinion, these are rare. The cerebrospinal axis may be affected directly by the presence of the organism in the nerve substance itself. It may be affected by gummatous infiltration of its enveloping membranes, the dura, arachnoid, or pia. It may be affected by gummatous disease of its blood supply. Or a combination of these three may exist. Thus it will be seen that the most varied symptoms referable to the nervous system may be produced, which, in a general way may be said to be either meningeal or non-meningeal, or a combination of both. The meningeal represent a more or less acute exudative process, whereas the non-meningeal represent a more or less chronic degenerative process.

Reproductive Organs.—Upon the reproductive functions of both sexes syphilis makes an indelible impression. While the Treponema pallidum has never been found in the semen, Finger and Landsteiner have proven conclusively that the semen of a syphilitic is infective. When a syphilitic woman becomes pregnant or a pregnant women becomes syphilitic a number of possibilities arise. A syphilitic woman, whose syphilis is old, that is in the tertiary stage, may give birth to a healthy child and this child may never show any evidences of the disease; or, it may appear seemingly healthy and yet show a positive Wassermann reaction, which later may become negative; or it may remain positive and in

from three to twenty years or even longer show evidences of the congenital form of the disease. Or it may be born with dystrophies which are undoubtedly syphilitic and yet show a negative Wassermann reaction throughout life. Or, a syphilitic woman may at one birth bear a healthy child and at the next, her disease in the meantime not having been influenced by treatment, bear a child with all the marks of congenital syphilis. As a rule, however, it may be stated that the older the syphilis the better are the woman's chances to bear a healthy child, although this by no means always holds good. A woman, who becomes syphilitic early in pregnancy, will, unless properly treated, abort, miscarry, give birth prematurely, or give birth to a syphilitic infant at term. If she becomes syphilitic late in pregnancy she may or may not give birth to a syphilitic child; and if the child is syphilitic it may or may not show signs of the disease.

Pregnancy.—Pregnancy undoubtedly enhances the local symptoms of syphilis, especially those about the external genitals. The disease and the pregnant state seem to exert a reciprocal influence on each other that is extremely deleterious to both. In so far as what may happen to the fetus, it is more serious in early syphilis than it is in late. The life of the fetus depends upon the intensity of the infection and the consequent degree of interference to its nutrition while *in utero*. This, of necessity, implicates the placenta, and the changes liable to occur therein in the active phase of the disease more intensely influence the fetal nutrition than when the dyscrasia is in abeyance or has become much attenuated. Although the placenta is the most frequent channel of infection for the fetus, it may be infected directly through the sperm of the father.

The syphilitic placenta is invariably heavier in proportion to the weight of the fetus than the normal placenta. The average normal proportion by weight between the placenta and the fetus is one to five or six, but in syphilis this proportion is reduced to one to three or four. This disproportion is due not so much to a relative increase in the weight of the placenta as to a decrease in the weight of the child, the result of nutritional disturbance caused by the placental disease.

It was formerly taught that the changes in the placenta in maternal syphilis were not definite or of diagnostic import. The more recent researches of Williams disprove this. In his opinion they are not only extremely characteristic but afford more conclusive evidence of the existence of syphilis than the demonstration of a positive maternal Wassermann reaction. In the placenta gummata are of rare occurrence. There is a diffuse infiltration of wandering cells, with vascular changes consisting of a thickening of the adventitia and the intima. In the villi there is a superabundance of loose connective tissue, especially surrounding the

central bloodvessel. This causes the villi to appear swollen and bulbous. The general infiltration also extends to the cord, causing it to be much thicker than normal.

Congenital Syphilis.—Congenital syphilis differs from acquired syphilis in that there is no primary lesion. The symptoms, as a rule, are more intense and in consequence they present a much greater variety and severity. The lesions may be present at birth or they may not occur for some weeks thereafter. As a rule, if the disease is active the lesions will appear within the first three months of life. If they are delayed until adolescence it is designated as *syphilis hereditaria tarda.*

In congenital syphilis there is to be observed an increase in the connective-tissue elements over the glandular. An exception to this, however, is to be found in the vascular system which is not so often attacked as in the acquired form of the disease. In congenital syphilis the treponemata are much more numerous and easier to find in the tissues than in acquired syphilis. Aside from the skin lesions of congenital syphilis which are usually papular and the lesions on the mucous surfaces which are identical with those in acquired syphilis, there are also decided changes in the bones, such as irregularities in the medullary canal, absence of the essential lime salts, periosteal infiltrations and gumma formation. Many syphilitic infants at birth show signs of pneumonia—the "white pneumonia" of Virchow. Such infants usually die within forty-eight hours and at necropsy show a cellular infiltration which may involve both lungs completely or in large patches. The alveoli are thickened and are filled with epithelium and leukocytes and mononuclear cells. The liver is enlarged in congenital syphilis, and if the case goes to necropsy it will be found to be literally swarming with the treponemata. The development of the organ is retarded so that at birth it is still a blood-making organ. There is capillary engorgement and continued new formation of liver cells.

The spleen and pancreas are enlarged by reason of the cellular infiltration. The hyperplasia of connective tissue in the kidneys causes more or less atrophy of the tubules and glomeruli and a similar hyperplasia is observed in the testicles.

The central nervous system is also gravely involved in congenital syphilis. Cellular infiltration of the meninges of the brain and cord, causing psychic and motor disturbances as exemplified by idiocy, hydrocephalus and various forms of paralyses, are included in the pathologic manifestations.

Gumma formation in all organs can and does occur. Histologically these do not differ from those seen in the acquired disease. The gumma, however, is not the characteristic lesion of congenital syphilis, but rather the gummatous infiltration which is identical with it except that it is diffuse instead of being circumscribed.

CHAPTER VI.

THE CHANCRE.

The chancre is the initial or primary lesion of syphilis. It represents the primary stage of the disease. If we except *syphilis d'emblée* it is always present in acquired syphilis.

Usually the chancre is single but it can be, and not infrequently is, multiple—in about 25 per cent of all cases. Occasionally the chancre is successive. That is, the first chancre is followed after a variable period by another. From the etiologic point of view these multiple chancres may be caused by the following: (1) A single source of infection, usually a syphilitic woman who inoculated the man in two places; (2) exposure to two or more women, all of whom were syphilitic and all of whom transmitted the infection; (3) the second, or successive chancre, may be derived from the first—this is usually due to the apposition of a mucous surface on the chancre—the so-called coaptation chancre. The coaptation chancre is the multiple chancre most frequently encountered, but this infection by continuity as it were is not especially characteristic of the primary lesion. It is well known that the mucous patch can cause another and similar lesion on a portion of mucous membrane in contact with it, and this holds good with other syphilitic lesions—the tubercular syphilide especially. It has also been noted that the period of incubation in these secondary chancres is practically the same length of time as in the original primary lesion.

The chancre is the result of an epithelial reaction to the Treponema pallidum and if the latter can be conveyed beneath the epidermis it will enter the blood and produce the disease without the concomitant of a chancre. This is *syphilis d'emblée.* Examples of this may be cited by the infection without chancre caused by a hypodermic needle or a cut from a scalpel. The French syphilologist, Gaucher, claims that a chancre can only develop on pavement epithelium which, of course, means the skin and continuous mucosa. Pavement epithelium does not absorb fluids unless there is a solution of the continuity of its surface. On the contrary, however, cylindrical epithelium readily absorbs fluids and consequently fluids containing infectious material. Because of this fact it is possible, and in my opinion it frequently happens, that a woman can become syphilitic and give birth to a syphilitic child because

of the entrance into the uterus, which is lined with cylindrical epithelium, of infected semen, without a chancre developing.

For many years it was considered impossible for syphilis to occur without the appearance of the initial lesion or chancre. But in 1897 Stassano called attention to numerous well-attested examples and proved that *chancre d'emblée* was a positive fact. The subject has been considered at length by Bettmann. It is, of course well established that a true *syphilis d'emblée* occurs when a fetus is infected by its mother, but the fact of its occurrence under other circumstances has been slow in gaining acceptance. Cordier asserts that its occurrence is quite common, not only in women, but in men as well. Certain it is that many syphilitics are absolutely unaware that they have ever had a chancre. In *syphilis d'emblée* it is to be noted that not only is the chancre absent but the usual adenopathy as well. *Syphilis d'emblée* has been known to occur in physicians treating syphilis when an infected needle happened to be stuck in the skin. It is also known that *syphilis d'emblée* occurs after a prophylactic circumcision.

I am in accord with Gaucher, who avers that fully one-third of the women who acquire syphilis do so by reason of a direct absorption of the Treponema pallidum through the vaginal mucosa. We know that syphilis can be conveyed by the intravenous route without the development of a chancre. It is, of course, possible in thus viewing the matter, to consider the possibility that the chancre occurs in the natural course of events, but that it is of microscopic proportions. It is well known that in women the chancre has not the typical appearance which it has in men. It is also not so apt to be indurated to the same extent as in men. In women also the sore is often so ephemeral and slight as to escape the notice of both the patient and the examiner. It is also peculiar that multiple chancres are much more frequent in women than in men.

A chancre may result either by mediate or immediate contact, as by sexual intercourse—the usual way—or by a kiss; or from a drinking glass or pipe. The period of incubation of the chancre varies from ten days to three months. The average period is about three weeks. Accompanying the chancre there is always some induration of the nearest lymphatic glands. This induration is always distinct—there is no matting of the glands as in tuberculosis—so that each individual gland can be distinctly felt. In the groin where this induration is most frequently met with, owing to the fact that the majority of chancres appear on the penis, there is produced a decided beaded effect—the so-called "Pleiades of Ricord." It must be remembered in connection with this, however, that in very thin individuals and those of powerful musculature and whose abdomens are free from fat, these glands can fre-

quently be felt in health. In patients past middle life the glandular enlargement is not so marked. It is a very rare occurrence for these glands to suppurate. When they do there is invariably some septic organism associated with the Treponema pallidum.

Rarely, if ever, is the chancre painful. Should, however, the chancre occur on the finger, as sometimes happens to surgeons and obstetricians, owing to the extensive nerve supply of the pulp of the finger and the root of the nail, it is painful from the onset. If the chancre, occurring on the penis, be irritated by the clothing or by dirt or by the application of caustic medicines it may become

FIG. 5.—Hunterian chancre. (Courtesy of Dr. M. B. Parounagian.)

painful. Left to itself without constitutional treatment, after a stationary period of varying length—usually from four to six weeks—the chancre heals. It will not spread or become phagedenic unless it has a chancroid grafted upon it, or unless the patient is debilitated from tuberculosis, alcoholism, diabetes, nephritis or malaria.

It is customary in text-books and the lecture room to describe a variety of chancres. In my opinion the differentiation of these various forms is of no clinical importance. They are all the primary manifestation of the same disease and vary in form rather than in kind. The opinion held by some—notably Ravogli and

McDonagh—that the degree of severity exhibited by the chancre is a criterion of the degree of severity that the future stages of the disease will display, is not, I believe, correct. There are certain characteristics, however, of the chancre which are necessary to know, and these I shall endeavor briefly to enumerate.

The chancre usually begins as a very small papule which soon turns to an erosion of a reddish varnished appearance. This erosion quickly becomes covered with a grayish-yellow exudate, which sometimes looks not unlike a diphtheritic membrane. The erosion is never excavated, but if anything is slightly elevated.

FIG. 6.—Hunterian chancre at the sulcus. (Courtesy of Dr. M. B. Parounagian.)

The inflammatory process is always distinctly circumscribed. An exception to this may be noted, however, in the rather rare chancre of De Maurignac, which instead of being confined to the immediately adjacent portion of the ulcer is more extensive and invades the surrounding tissue for some distance, producing an inflammatory edema of large proportions compared to the actual size of the lesion.

When it first appears the chancre is not indurated, it is not "hard," it has not the "shot-like" feel, nor does it feel like a "split pea;" all of these descriptions have been applied to it. Rather it

is because of this lack of hardness at the beginning, that the inexperienced (because they have been led to believe that every chancre is "hard" from the beginning) so often make mistakes in diagnosis. The induration which is characteristic comes on slowly. It usually takes from ten to fourteen days before it becomes a diagnostic feature. It is to be understood, therefore, that in any suspicious sore absence of hardness is by no means negative of syphilis. For this very obvious reason any sore on the genitals, even the seemingly benign excoriation of a ruptured herpetiform vesicle should be viewed with suspended judgment whenever a history of a suscious coitus has been given.

FIG. 7.—Chancre of the meatus. (Courtesy of Dr. M. B. Parounagian.)

These fundamental characteristics of the chancre just described may assume a number of forms upon which some clinicians lay considerable stress. I have already discounted this, but as an aid to diagnosis it may not be out of place to describe them. The most common form of chancre is the erosion. It appears exactly like an excoriated spot, the surface of which is on a level with or slightly elevated above the level of the surrounding parts. It is red in color and later may take on a darker and more coppery hue. This form of chancre is most frequently seen on the internal surface of the prepuce. Usually it is round but it may be irregular in shape. It is the form of chancre that is most often mistaken for herpes progenitalis or a chafe from some mechanical cause. The erosive chancre may ulcerate, the ulceration being either superficial or deep. If the ulceration is superficial there is a depression caused

by a partial destruction of the skin or mucous membrane as the case may be. The edges of the ulcer slant and its floor is covered with a grayish membrane. Deeply ulcerated chancres are fairly frequent. The whole of the skin or mucosa is destroyed as well as the tissues beneath, making a deep excavation surrounded by a ring of cartilaginous hardness. This is the "Hunterian chancre" and represents the classic sore. Sometimes the chancre does not erode but remains a papule until resolution takes place. The surface presents a bright red, glazed appearance and if the underlying induration is thin it is sometimes spoken of as a "parchment"

FIG. 8.—Rosette chancre. (Courtesy of Dr. M. B. Parounagian.)

chancre. Should the induration dip deep into the tissues it is called an indurated nodule. Some chancres become quickly covered with a crust of dried pus of a brown or greenish-yellow color beneath which is a red, beefy sore. This is the so-called "beefsteak" chancre; and it is usually of considerable size. The mixed chancre is one which has grafted upon it a chancroid. The chancroidal sore appears first and it is only after several weeks that the induration of the syphilitic lesion is made manifest.

After healing the chancre usually leaves a scar and the induration also persists for a long time—sometimes for six months. This

is so even under treatment. In many instances, however, when the erosion has been small and the induration slight, this after-hardness does not occur and the chancre once healed leaves no trace.

It can be readily understood why it is of the utmost importance that an absolute diagnosis of a chancrous lesion be made as soon as possible after its appearance. The prompt recognition of the character of a suspicious sore has much (if not all) to do not only with the local treatment, but also as to the cure of the constitutional

Fig. 9.—Chancre and squamous psoriasiform eruption. (Courtesy of Dr. M. B. Parounagian.)

disease should the lesion prove to be syphilitic. It is necessary, therefore, to be able to differentiate between certain lesions with which the chancre may be confused.

Chancroid.—Of these the most common and at the same time the most difficult to diagnose, especially to those who are not constantly in contact with them, is the soft sore or chancroid. The chancroid is a purely local infection caused by the streptobacillus of Unna-Ducrey. Unlike the chancre the chancroid has no period of incubation. It appears at once after inoculation; whereas it is at least ten days before the chancre appears. From the beginning

the chancroid secretes an abundant amount of pus; this the chancre does not do. The chancroid is a deep, clear-cut, excavated ulcer with undermined edges; the chancre is smooth or only slightly elevated. The chancroid shows a decided tendency to spread—which the chancre does not. Surrounding the chancroid is an inflammatory areola; this is not present with the chancre. The underlying mass of the chancroid lacks the cartilaginous hardness of the chancre. It feels brawny, like a carbuncle, rather than like

Fig. 10.—Multiple chancroid. (Courtesy of Dr. M. B. Parounagian.)

an imbedded piece of gristle as does the chancre. Accompanying nearly every chancroid, unless vigorously treated from the onset, is a suppurating bubo; a suppurating bubo is never seen with a chancre, unless it is complicated with a pus-forming organism. The chancroid is autoinoculable, which the chancre is not except on the mucous surface in apposition to it and that not after ten days. The chancroid sometimes assumes a serpiginous or an acneiform aspect; in chancre this does not occur. Finally, the chancroid is more apt to become phagedenic than the chancre.

Herpes Progenitalis.—Another condition common on the penis, and which is sometimes mistaken for chancre, is herpes progenitalis. This condition not infrequently causes needless alarm to the patient. But it is to be borne in mind that as the chancre sometimes begins as a slight and seemingly insignificant sore these eruptions should always receive attention. Herpes progenitalis is frequently seen in those patients of sexual neurasthenic tendencies who spend a considerable part of their time in examining the state of their penis. Herpes usually appear in crops of small, almost minute blebs or vesicles, not indurated and not eroded. Sometimes these crops, because of uncleanliness or from other cause, become eroded and confluent. It is then that the suspicion of chancre is most apt to be entertained.

Scabies.—Scabies occurring on the penis may also be mistaken for chancre. In discriminating between chancre and scabies it is to be remembered that in scabies there is no induration, no period of incubation and no adenitis. The lesions of scabies are multiple and scattered over the rest of the body as well, and the itch mite can almost invariably be found if carefully sought for.

At any time subsequent to the healing of the chancre a sore similar in appearance may again present itself upon the original site. It may not erode but exist simply as an induration. It runs an indolent course and if showing within two or three years after the primary lesion may be accompanied with glandular enlargement. In some instances it becomes quite large and is usually very rebellious to treatment; in this last respect it differs from the original sore. This is the *chancre redux* or "relapsing chancre." It is not infrequently mistaken for a second infection, but this error is now less liable to be made than formerly, because of the Wassermann reaction which is rarely positive when the chancre first appears but which in the event of a chancre redux would almost invariably be so.

Chancre redux is not to be confused with relapsing pseudo-chancre after arsphenamine: a phenomenon which has been observed with more or less frequency since the introduction of that drug. It not rarely happens after a chancre has healed under arsphenamine that a new sore after a time develops on the site of the first. At first it is about the size of the original lesion, but it soon increases in size until it is as large as a half-dollar or even larger. It may be surrounded by smaller ulcers. The ulcer is round or oval in shape, regular and clean cut in outline, with a smooth or slightly granular floor, and is covered with a grayish white pellicle which readily comes away. There is little or no adenopathy. These ulcers are quite benign. They last for a few weeks and usually heal spontaneously. Occasionally it is necessary to administer mercury to

cause them to resolve. As a rule, the ulcer is free from treponemata although they are sometimes found. This type of ulcer is not a true chancre redux, although one would classify it as such, nor can it be called a reinfection. The probable explanation for its appearance is that it represents a local reaction to the arsenic contained in the arsphenamine.

Diagnosis of chancre by means of direct examination for the presence of the Treponema pallidum is coming more and more into vogue. It is undoubtedly a most excellent practice, but I want to caution the reader that in many sores which are indubitably syphilitic but few treponemata exist, and these few may be easily missed. When treponemata are found it is further necessary to differentiate them, for there are other treponemata besides the Treponema pallidum. The Treponema refringens and the Treponema balanitidis are those which are most apt to cause confusion in diagnosis. The most accurate and also the simplest method for detection of the Treponema pallidum is by means of the dark-field illumination. Before an examination is made it must be ascertained whether the patient has used any antiseptic powder or ointment. If such be the case it is useless to make a dark-field examination as the organisms will be destroyed by the treatment. The patient should be instructed to return in a week, meanwhile abstaining from further local treatment.

The lesion to be examined for treponemata should be thoroughly cleansed with a pledget of cotton, and a drop of serum expelled by squeezing and allowed to fall on the slide or cover-glass. The serum should be clear. When contaminated with blood or pus the numerous cells present will greatly hinder the detection of the treponema. The search for treponemata in fresh serum is not so difficult, although considerable experience is necessary before anything like accuracy can be secured.

CHAPTER VII.

EXTRAGENITAL CHANCRE.

It is most important to bear in mind that syphilis is not necessarily acquired by sexual contact. It is quite possible to acquire the disease elsewhere than on the genital organs. It is also quite possible for the disease to be transmitted by direct inoculation of the treponema into the blood or lymphatic streams without the previous appearance of a chancre. That this is so has been proven by animal inoculations. The term extragenital chancre connotes the appearance of the primary lesion on other parts of the body than the genitals. Syphilis acquired in this manner has been known since very early times. Authentic epidemics of "syphilis insontium" or syphilis of the innocent, that is, syphilis acquired in some other (and innocent) way than by coitus, were reported as early as 1577 in Austria, in 1592 in Switzerland and in 1596 in Germany. Most of these early reports showed that the disease resulted from scarifying, phlebotomy, breast-drawing, or lactation.

Primary syphilis on other parts of the body than the genitals is rather rarely encountered by the general practitioner. Yet, I dare say every man of extensive experience has met with it in his practice.

Frequency of Extragenital Chancre.—L. D. Bulkley has collected 9058 instances of extragenital infection. Of these 20 per cent were on the lips; 12.5 per cent on the breast; 5 per cent on the hands, and the remainder were distributed to almost every conceivable part of the body. The lesions are sometimes placed so unexpectedly, and so remote from the usual site, that the question arises how the infection could possibly have occurred.

In his private practice, Bulkley noted 113 cases of extragenital chancre. Fifty of these were on the lips; 15 on the tonsils; 15 on the fingers; 7 on the breast; 7 on the tongue, and the rest were distributed on other parts of the body. It will be noted that 72 were on or in the oral cavity. In this respect Bulkley's experience coincides with my own. Most of these infections were contracted from dishes, towels, drinking-cups and kissing. Several of them, however, were contracted in a manner quite out of the ordinary. For example: A young woman, after being stung by a bee, allowed a male friend to place a piece of court plaster over the sting which he first moistened with his lips. A chancre resulted. A similar

case has been reported by Ricord: An old gentleman played the part of the good Samaritan to a little boy whose head was cut while at play. Mucous patches in the old man's mouth caused the child to contract syphilis. Schamberg has reported the case of the champion kisser of the city of brotherly love who infected 9 young women by his osculatory caresses.

Montgomery has reported 7 cases, of which 6 were on the hands. Out of 20 cases reported by Brandis and Morrow, 6 were on the hands and had been contracted by physicians in gynecological and obstetrical cases. In a series of 49 cases reported by Fournier, 30 were in physicians who had contracted the disease in the course of their professional duties. Cole, of Cleveland, reported 61 cases, of which 43 occurred on the lips; 3 appeared on the tonsil; 1 on the tongue; 10 on the hand; 1 on the neck; 1 on the jaw; 1 on the abdomen; 1 on the breast. Bites were responsible for 4 cases; kissing in 9; a razor in 2.

Fournier gives the following locations of 1124 extragenital chancres: On the lips, 567; the tongue, 75; tonsils, 69; gums, 11; the buccal cavity, 5; chin, 54; the cheeks, 24; the eyelids, 21; the nose, 18; the forehead, 2; the scalp, 3; the arms and hands, 78; the anus, 77; the breasts, 59; the trunk, 33; the thighs and legs, 14; the neck, 14. The modes of transmission in many instances of extragenital chancres are so strange and bizarre that it is almost impossible to discuss them.

It is manifestly impossible to determine with any degree of accuracy the comparative frequency of extragenital infection. The statistics of hospitals are far from accurate, especially where the different branches or specialties are conducted independently. Unless there is a well-maintained correlation between these departments the statistics in many instances conflict in a way that is most confusing. As a rule, if the patient in applying for treatment states that he has a sore on his penis he is at once referred to the department of genito-urinary diseases and, *a priori*, a diagnosis of syphilis is made. But on the other hand, if the patient states that he has an eruption on the body, he is referred to the dermatologic department, and if syphilis is suspected he will be questioned as to the presence of a chancre if none be found. Thus, if the disease is extragenital it is more apt to be discovered in the dermatologic department than in the genito-urinary.

According to Julien, extragenital chancres occur in 2 per cent of all cases of primary syphilis. It is also stated on good authority that extragenital chancres are more frequent in Italy and Russia than in other countries where syphilis is prevalent.

From the method of infection extragenital chancres may be

divided into two classes: (1) When they are innocently acquired, as from a drinking glass or an infected razor; (2) in contradistinction to these innocent ways of acquiring the disease is the acquirement of the chancre by means of perverted sexual practices. Chancre acquired by sodomy or buccal coitus are examples of acquiring the disease in this manner.

Infection with syphilis occurring in physicians is much more frequent than personal experience and statistical data indicate. Surgeons, obstetricians and gynecologists are particularly liable to the extragenital form of infection as many melancholy instances show.

Syphilis Brephotrophica.—Unspeakably sad is the fate of the child which accidentally contracts lues. The sources of infection are almost too numerous to mention. The disease is not infrequently communicated by some act pertaining to the care and feeding of infants and small children. The name *syphilis brephotrophica* (*βρέφος*, babe, and *τρέφειν*, to nourish) has been given to syphilis thus acquired. In the days before the Wassermann reaction, infants were often infected by wet nurses; and the literature of former times contains many instances of this kind.

Included in syphilis brephotrophica is infection occurring during parturition; which should not be confounded with congenitally acquired syphilis. Although such infection has been questioned there has been sufficient evidence produced to admit its possibility. It can be readily understood how contact of the forecoming head with mucous patches in the mother's vagina or vulva can cause such an infection. Grünfeld has reported a case of an infant three weeks old developing a chancre on the scalp, followed in six weeks by secondary symptoms. Weil has reported a case of an infant in which a chancre at the root of the nose appeared four weeks after birth. In both of these cases the mothers had contracted syphilis late in pregnancy and the vulva of both showed numerous mucous patches.

Many instances are on record of syphilis having been transmitted by adults to infants while sleeping in the same bed. Trousseau has given the details of a case where a male infant of four months had a chancre on the buttock acquired from mucous patches on the mother's vulva, the infant being in the habit of going to sleep with its buttocks against her abdomen. Pellizzari observed a case where a nursling acquired a chancre of the lower eyelid from contact with the secretions of its mother's mouth in which were mucous patches. The mother had recently acquired syphilis and had exercised great precaution against the infection of the infant. The infant slept with her for but a single night, but on this par-

ticular night she fell asleep with the infant in her arms and upon awakening found its forehead bathed in her saliva. A chancre resulted.

Artificial Feeding.—Numerous cases have been reported following the artificial feeding of infants. Boeck has reported a case in which an infant was infected with a chancre of the buccal cavity by a nurse who partially masticated its food before feeding to the infant. Sigmund and Plumbert have reported infections from using sugar teats, previously sucked by luetic infants.

Kissing.—The infection of children and infants by kissing is a most frequent mode of infection. Many instances are on record of the disease having been transmitted to children in this manner.

Syphilis and Vaccination.—Formerly syphilis was frequently conveyed by vaccination. When human virus was used it is safe to say that it gave rise to more epidemics of syphilis than were derived from any other source. Pacchiotti reported an epidemic of vaccinal syphilis that occurred in the town of Rivalta in Italy, in 1861, where eighty persons were thus infected. In vaccinal syphilis the period of incubation was said to have been much shorter than when the disease is contracted in some other way. Since the advent of bovine virus for vaccination purposes it is now hardly ever encountered.

Syphilis and Circumcision.—Although syphilis acquired through the rite of circumcision can hardly be classed as extragenital, yet in times past it has undoubtedly caused syphilis insontium, as many observers have noted. In order to avoid the possibility of such infection the sucking of the wound caused by the circumcision knife has been abolished as a part of this ancient Hebraic rite.

Syphilis d'emblée.—*Syphilis d'emblée* is the term that has been used for years past to describe that form of syphilis which occurs without the presence of the primary lesion. The possibility of syphilis being so acquired has long been recognized, and there are reports of its having occurred as far back as the sixteenth century. In 1728 Vella wrote that a solution of continuity was not necessary for the penetration of the syphilitic virus, that the disease could be acquired without any lesion of a primary character whatsoever. This belief was also held by Mathiolus Fallopius, and Thierry de Hery.

In 1897 Stassano expressed the opinion that many cases of syphilis occur without a primary lesion and that a solution of continuity is not necessary, as shown by the occurrence of chancres on the tonsils where such solutions of continuity could hardly occur. Stassano even goes so far as to consider the primary lesion as a part of the secondary eruption because of the absence of any sign at the situation of the chancre during the period of incubation.

With this view I am not in accord. In regard to *syphilis d'emblée* Hutchinson writes as follows: "However definitely as a matter of pathologic accuracy we may repudiate the notion that acquired syphilis can ever begin without its initial lesion, yet for practical purposes we are obliged to admit that there are cases in which the primary sore wholly escapes notice." The phenomena which characterize a chancre are probably to be met only on the cutaneous or mucous surface. If the parasite gains access to the deeper parts it is quite possible that it may also gain access to the lymph channels and the blood without producing any local changes.

Syphilis d'emblée has also been carefully considered by Almkvist and Gottheil, both of whom consider it extremely rare. With this I do not agree as I am of the opinion that *syphilis d'emblée* occurs with much greater frquency than is usually supposed. This opinion is also, I believe, shared by Fordyce.

In contradistinction to *syphilis d'emblée* or syphilis without a primary lesion, there are instances where the chancre, although present, is so obscurely located that it entirely escapes the notice of both patient and physician and is discovered usually by accident. Examples of this are chancre of the cervix uteri and chancres located in the urethra. The patient is unaware of the occurrence of a chancre or even of contact with anyone who has syphilis. These mysterious infections are called cryptogenic syphilis. There is very little in the literature concerning syphilis acquired in this manner. Lane has described six cases. It would seem that syphilis so acquired is characterized by the absence of glandular enlargement, otherwise its course is identical with syphilis acquired in the usual way. The reason for this is that in ordinary syphilis the treponemata are imprisoned as it were in the lymph glands and only gradually escape into the blood stream and so produce the secondary symptoms, whereas in *syphilis d'emblée* and to a lesser extent in cryptogenic syphilis the treponemata are introduced directly into the blood and thus for the nonce the lymphatic glands escape and the secondary symptoms appear at once. It is also said that this form of syphilis runs an unusually severe course, but this may be due to the fact that the disease goes so long unrecognized that the treponemata have the opportunity to work considerable havoc before they are arrested by treatment.

Chancres appearing on other parts of the body—extragenital chancres—are influenced more or less by their situation. As a rule, the size and elevation of the chancre under these circumstances is directly proportionate to the thickness of the skin. The infiltration is usually greater, but the induration is not so marked.

It is believed by many that extragenital chancre presages a severe form of the disease. With this view I am not in accord.

Some twenty years ago the elder Fournier investigated the subject most thoroughly. His conclusions are of the highest value in dispelling this ancient fiction of severity following extragenital lesions. Fournier began by assuming tertiarism to be a criterion of severity, and his deductions were made accordingly. He analyzed 1200 cases of tertiary syphilis and found that of this number the primary sore was extragenital in 75. This is a ratio of about 1 to 14. But—and this is important—he also noted that the ratio of tertiarism is exactly the same in chancres appearing on the usual site. It is undoubtedly true that the term tertiarism as applied to syphilis is a somewhat elastic conception. It is well known that tertiary symptoms may develop only after the lapse of many years, or they may appear within a few months of the initial lesion. Again, should we regard that form of tertiarism known collectively as "nervous syphilis" as a criterion of severity? In the opinion of the writer and of all syphilologists with whom he is acquainted there is no form of syphilis so terrible as syphilis of the nervous system. Fournier evidently thought so, else he would not have approached the subject from that angle also. Assuming nervous syphilis to be an evidence of severity, what did he find? Not an increased ratio, but, on the contrary, a ratio that was markedly diminished—1 to 20. It would seem, therefore, that extragenital chancre reduced the chances of the infected individual developing nervous syphilis. My own experience agrees in the main with Fournier; hence, I am safe in saying that the constitutional effects following extragenital infection in no way differs from that occurring on the genitals. Before dismissing the question of severity and extragenital infection it might be well to state that an extragenital chancre in some localities undoubtedly conveys the impression of increased severity. This is particularly so of chancre of the tonsil, which is often accompanied with considerable constitutional reaction, such as fever, chills, headache, myalgia and dysphagia. The cause of this is a mixed infection and the anatomic site of the lesion. Chancre of the tonsil is not infrequently mistaken for diphtheria or Vincent's angina; especially the latter, as Vincent's angina is caused by a treponema closely resembling the Treponema pallidum.

Chancre of the Finger.—The most frequent extragenital sore is that occurring on the finger. Chancre of the digit is often mistaken for a felon or whitlow. Nor is it hard to understand why this mistake in diagnosis is so often made. When occurring on the fingers of physicians, midwives or nurses it is in nearly every instance the index finger. When the result of obscene contact it is usually the middle finger. As might be supposed, the fingers of the right hand are more frequently affected than the left. When a chancre occurs on the finger, the part becomes red, swollen and

painful. The swelling may reach such a degree as to cause the finger to assume the shape of a pear or a sausage. Because of this appearance of intense edema, a suppurative process may be suspected and the lesion, in consequence, incised. Since this procedure is not attended with the evacuating of pus it may not be until constitutional symptoms intervene that the real nature of the lesion is discovered. In some instances chancre of the finger takes on a fungoid appearance which, while not characteristic of chancre occurring elsewhere, offers less difficulty in diagnosis than when it represents an infection of streptococcic or staphylococcic origin. The evolution of chancre of the finger is very slow. It usually persists for two or three months or even as long as a year. It is also to be noted that even after healing has taken place the finger is indurated and enlarged for a long time afterward. In women and children chancre of the finger is hardly ever seen.

FIG. 11.—Chancre of the thumb.

Chancre of Nipple.—Chancre of the nipple sometimes occurs in women who have suckled a syphilitic infant. When so caused it is always bilateral, *i. e.*, the lesion appears on both nipples. The usual point for its appearance is at the papillary base, in the fold between the nipple and the areola. These lesions are nearly always multiple and not infrequently they coalesce and form an ulcer of considerable size. The lesion may, however, be single and of very minute appearance. In chancre of the nipple the axillary glandular enlargement is, as a rule, but slight. Primary syphilis occurring on this location is not infrequently mistaken for fissure, epithelioma and Paget's disease.

Chancre on the Lip.—The lip is a frequent site for chancre to occur—the upper lip more often than the lower. Clinically it presents no distinguishing features. If exceptionally large and of a "beefy" appearance it may be mistaken for epithelioma. Labial

chancre sometimes shows a tendency to ulcerate, and may be attended with a considerable loss of tissue. Strange to say, however, after it has healed it does so with hardly a sign of scar tissue. Chancre of the lip occurring at the labial angle is nearly always erosive. It sometimes becomes quite large and is slow to heal, being kept open by the movements of the lips. Occasionally chancre of the lip is so small and insignificant that it is mistaken for a herpetic vesicle. The cracks and fissures that occur on the lips often simulate chancre very closely and have been mistaken for such by observers of wide experience.

Fig. 12.—Chancre of the lip. (Courtesy of Dr. M. B. Parounagian.)

Chancre on the Tongue.—Occasionally a chancre occurs on the tongue. It is invariably single and occupies the upper and anterior surface of the organ. It is usually oval in shape and looks as if the papillæ were scraped away in a circumscribed area corresponding to the location of the sore. Occasionally it is covered with a grayish exudate which gives it the appearance of a mucous patch such as may be seen in the secondary stage of the disease. Chancre of the tongue is characterized by excessive induration which frequently causes it to be mistaken for malignant disease. In the differential diagnosis between these two conditions it is to be noted that malignant disease is not often seen in patients under forty years of age. It is also extremely rare in women, except East Indian women who chew betel. When it occurs in men there is usually a history of heavy smoking. Epithelioma bleeds very easily, even the merest touch will cause it to bleed. The surface of an epithelioma is covered with vegetations. The adjacent lymphatic glands enlarge only after a considerable lapse of time. There is no generalized eruption as would be the case if the lesion

were a chancre. Epithelioma does not respond to the therapeutic test.

Chancre of the tongue, however, is most apt to be mistaken for tuberculous ulcer. The diagnosis between the two lesions is

FIG. 13.—Chancre of the tongue. (Courtesy of Dr. M. B. Parounagian.)

sometimes extremely difficult. In not a few instances recourse must be had to the microscope or to the serological or therapeutic

FIG. 14.—Chancre of the tongue. (Courtesy of Dr. M. B. Parounagian.)

tests. It is worthy of note in distinguishing between chancre and tuberculous ulcer of the tongue that the chancre is invariably single while the ulcer of tuberculosis is apt to be multiple. Tuberculous ulcers are also larger and excavated, whereas the chancre is

never excavated. Tuberculous ulcer is attended with pain, which is not a marked symptom of chancre. Tuberculous ulcers are often seen under the tongue where the chancre hardly if ever occurs.

Circumscribed ulcerative glossitis sometimes resembles chancre very closely, but it quickly disappears when the offending tooth which is the cause of the irritation is removed.

Ano-rectal Chancre.—Chancres occurring about the ano-rectal region are frequently overlooked. Their incidence is about equally divided between males and females. In males it is not infrequently due to pederasty. In females it is usually found only in the lowest class of prostitutes. These chancres have no distinguishing characteristics inasmuch as they are identical with a chancre occurring on any cutaneous surface. Chancre occurring within the sphincter, that is, within the rectum itself, is of such rare occurrence that it is impossible for me to describe it.

Chancres on the Face.—Chancres on the face—the cheeks or chin—are rare. They are usually caused by bites or kisses given by an infected individual. The lesion is usually single. Occasionally, however, they are multiple. In view of the fact that chancres of the face are, perforce, cutaneous lesions, they do not differ from those occurring elsewhere on the integument. The diagnosis is made from the general appearance of the sore, its slowness in healing and the accompanying adenopathy. In some instances a history may be obtained which helps to clear the diagnosis.

Chancres have been known to occur on the scalp, the ear, the nose, the neck, the trunk and the arms and legs. The mode of transmission in many instances is so strange and bizarre that discussion is impossible. Not infrequently, especially on the arms and trunk, they have been caused by tattooing.

The non-venereal transmission of syphilis—*lues sine coitu*—is an ever-present possibility which must at all times be reckoned with. The portals, through which the disease may enter, are as numerous as the relations of daily life. *Latet anguis in herba. Videat et medicus et laicus.* Truly, is the ubiquitous, the insidious treponema "the pestilence that walketh in darkness—the destruction that wasteth at noonday."

CHAPTER VIII.

THE SECONDARY STAGE OF SYPHILIS.

Secondary Incubation.—Following the appearance of the chancre there is a period during which there are no constitutional symptoms. During this seeming quiescence the treponemata are increasing and spreading, and when sufficiently disseminated the secondary explosion occurs. This secondary incubation, as it is called by some, is of variable length—a month—six weeks—six months sometimes. It is usually about six weeks. In an appreciable number of cases secondary symptoms never occur; or else, they are so fleeting and ephemeral that the patient has no cognizance of them, and in after years his denial of them is no evidence of bad faith. Should the patient be put under arsphenamine and mercurial treatment as soon as the chancre is diagnosed there may never be any secondary manifestations of the disease or they may be very much delayed. In some instances, when for some reason treatment is stopped too soon, a peculiar roseola appears. This eruption differs somewhat from that which occurs when treatment has not been given. The rash of untreated secondary syphilis covers the entire body—no part escapes. The delayed rash is not so widely distributed. It appears as relatively large macules of uneven and limited distribution, which are somewhat slow to disappear. The probable reason for their being is that the toxicity of the infection has not been attenuated sufficiently, and hence this abortive display.

Prodromal Fever.—In a considerable number of cases, but by no means in all, there is a prodromal fever before the appearance of the eruption. This fever partakes more of the nature of a hectic rather than of a continuous fever. It has sometimes been mistaken for the so-called "walking typhoid," and again, when the roseola was present, for typhus. When a widespread pustular eruption was present with the concomitant fever and symptoms of sepsis, syphilis has been mistaken for variola. Keyes notes that with the fever bulimia is present, but this I have never observed. The fever precedes the eruption by a week or ten days. It is in fact the first manifestation of the generalized toxemia. Often at this time and for some time after the establishment of the eruption, unless controlled by treatment, the patient complains of lassitude,

malaise and vague pains. The patient loses weight; and this loss of weight is almost invariable. At this time there is observed a systemic enlargement of the lymphatic glands which may be easily palpated in the neck, the axilla, the popliteal space and at the elbow. In not a few instances this general glandular enlargement is the only symptom of the constitutional character of the disease. Again the glandular enlargement may be so slight as to make its discernment somewhat difficult. In phthisical or otherwise debilitated individuals the prodromal fever, malaise and loss of weight are apt to be more marked than when occurring in those who enjoyed previous good health.

Eruption.—The exanthemata follow the fever. There are some syphilologists who deem it advisable to enumerate a long and more or less complicated list of syphilodermata, which in my opinion only adds to the confusion of the reader, especially if he is not an experienced dermatologist. That the skin lesions of syphilis are numerous and varied is undoubted, and it is equally true that they can simulate any skin disease known. But for practical purposes they can be divided clinically and histologically into three groups—macular, papular and tubercular.

Syphilitic skin lesions of the secondary stage have certain characteristics which are worth remembering and if these patent facts are borne in mind difficulties in diagnosis will be much reduced. These characteristics are, that syphilitic skin eruptions are almost invariably free from pain and itching. But in this connection it must not be lost sight of that a syphilitic dermatosis may be superimposed upon a pruritic dermatosis that existed before the syphilis was contracted. Scabies and eczema are the two pruriginous skin diseases with which the cutaneous lesions of secondary syphilis are most apt to be complicated. The rash in secondary syphilis is always symmetrical and it follows the direction of the skin fibers. Thus, on the back the eruption is disposed in parallel rows running obliquely downward. Also, whether appearing singly or in groups the eruption assumes a round or elliptical form, following the course of the dermal blood supply. This tendency toward circular forms, either as complete circles or segments thereof is more characteristic of syphilis than any other skin diseases except tinea circinata. Polymorphism is another permanent characteristic of secondary skin eruptions; so much so that it may be looked upon as pathognomonic. Rarely, if ever, is there any skin eruption in the secondary stage that has existed for several weeks that does not show the three, or at least two of the eruptive types already mentioned, concurrently present, or one developing within the other—macules changing into papules, or a papule encompassed by pustules, or all three scattered over the body. In many

instances the rash spares the face while it is generalized over the rest of body. It may, however, be extremely marked at the junction of the cutaneous surface of the forehead and the hairy scalp where it forms the so-called *corona Veneris,* or "crown of Venus."

Macular Eruption.—The macular type of the eruption is divided into the roseola and the large macular syphilide. In by far the greatest number of cases the roseola is the earliest rash to appear. It is most important to recognize it as it may often be the only sign of syphilis present. The roseola is nothing more than a hyperemia

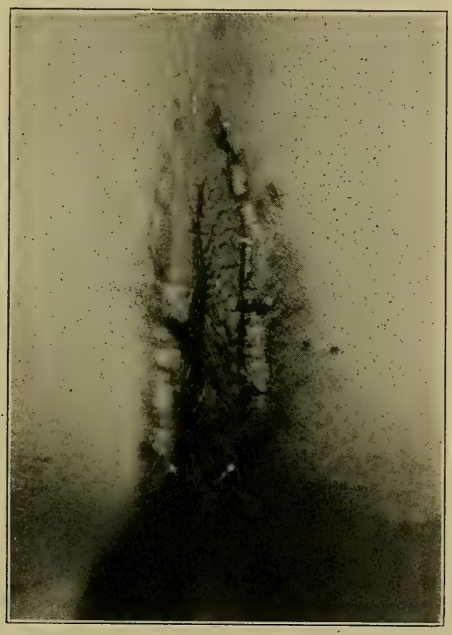


FIG. 15.—Condylomata. (Courtesy of Dr. M. B. Parounagian.)

of the skin. It usually begins on the abdomen or thorax and may later cover the entire body. The face may escape, also the dorsal surfaces of the hands and feet. Not infrequently it is very faint and evanescent and may entirely escape the attention of the patient. The eruption when sufficiently noticeable is of a brownish-red color and on a level with the surrounding skin, although it may in some instances be very slightly elevated. The lesions are usually about 1 cm. in diameter, although they may vary in size—sometimes miliary, and again much larger. In from five days to two weeks the roseola fades away and leaves no trace. Occasionally it recurs;

that is, a second and even a third and fourth eruption may appear at varying intervals.

The large macular syphilide is of later appearance that the roseola, which is often its forerunner. This syphilide is distinctly coppery in color and thus has given rise to the so-called "copper-colored spots" popularly associated with syphilis in the minds of the laity. The large macular syphilides are slightly raised above the level of the skin and sometimes show a slight desquamative tendency. They persist longer than the roseola and upon disappearing sometimes leave a pigmented spot or, there may be absence of

FIG. 16.—Condylomata. (Courtesy of Dr. M. B. Parounagian.)

pigment, which if the macules have been at all numerous will give rise to the so-called cutaneous leukoplakia.

Papular Eruption.—The most frequent secondary syphilitic eruption is the papule. It is often combined with macules and pustules. These nodules of the skin and mucous membrane vary much in size—ranging from a millet seed to a lima bean. When they first appear they may be found all over the body; but after the disease has become chronic, they become less diffused and are localized more or less about the genitals and anus, the palmar and plantar surfaces and the buccal mucous membrane. When about the anus and the genitals, especially in females, they take the

appearance of flat, warty growths and are designated as condylomata lata. When appearing in the mouth and on the larynx and tonsils and the glandular surface of the prepuce and in the vagina they are known as "mucous patches," which as such, are so often mentioned in the literature and conversation on syphilis. In view of the fact that these lesions are not strictly limited to the mucosæ the term moist papules, or syphilomycoderm, as suggested by Thompson, would seem more appropriate. These moist papules may consist of mere abrasions, such as fissures or rhagades, or they may appear as superficial ulcers, or they may be present as a primary hypertrophy which later undergoes a loss of substance through ulceration.

These lesions above all others are characteristic of syphilis in the secondary stage. They appear very early after the eruption and in many instances they may even precede it. They are highly infectious and from them the vast majority of infections are incurred. Unless the disease is vigorously treated they may continue to appear for several years—I have seen them recur fifteen years after the initial lesion. In some individuals they are extremely rebellious—hard to cure and prone to return. They may relapse spontaneously or from irritation such as bad teeth and the use of tobacco in men, and gonorrhea and lack of cleanliness in women. Mucous patches on the pillars of the fauces, the tonsils or the soft palate may simulate diphtheria very closely. They are to be differentiated from the latter by the absence of fever, their indolent course, the previous history and the evidences of syphilis elsewhere and by the presence of the Treponema pallidum instead of the Klebs-Loeffler bacillus. When the tonsils are affected there is dysphagia caused by the angina; the voice takes on a peculiar nasal tone and there is frefrequently an excessive flow of saliva.

On the dorsum of the tongue the papule sometimes appears as a slight elevation from which the superficial epithelium has been denuded, giving it the appearance of a bright red spot or patch or as if the tongue had been scratched. The papules may also appear on the vulva and become confluent so that the entire surface seems raw and denuded. Should they become infected with pyogenic organisms, as frequently occurs on the genitals of uncleanly women, they may ulcerate extensively, or the excoriated papillæ may hypertrophy and exude a foul and fetid secretion that is extremely offensive.

Pustular Eruption.—The pustular syphilide rarely occurs as a first eruption; it is usually preceded by the macular or pustular forms. When it does appear primarily it predicates a severe type of the disease. Pustular syphilides are naturally accompanied with symptoms of pus infection—headache, chills and sweats and more

or less prostration. In extremely rare instances the pustular syphilide develops from a primary vesicular or bullous syphilide. The existence of the last two lesions has been denied by some, but I am convinced that they do occur, although they are extremely rare.

These pustules may be large or small, that is miliary or acneiform. They may show a slight umbilication at the summit, although this is by no means a uniform feature. They are apt to be abundant and widely scattered. The pus contained therein sooner or later dries and forms a crust, which is increased by successive layers until a raised, laminated mass is formed beneath which is a raw surface. These lesions are called rupia and are not infrequent in run-down and dissipated individuals in the later secondary stage. They occur usually upon the anterior aspect of both legs. Lesions closely resembling psoriasis are among the late secondary eruptions. There is also a nodular syphilide which may closely simulate lupus, especially when it appears upon the face. Chronic, dry exfoliative lesions sometimes appear on the palms of the hands and the soles of the feet. They are extremely rebellious to treatment and may be the only cutaneous manifestation of the disease. These palmar and plantar syphilides are supposed by some to presage involvement of the nervous system. I am not prepared, however, to accept this view.

Malignant Ulceration.—In secondary syphilis, malignant precocious syphilides of an ulcerative character may occur, usually in weak, cachectic individuals. They present three distinct varieties. The first is a pustular rash with considerable ulceration and the formation of scabs. The second begins as red tubercles, the size of a pea which rapidly ulcerate and become covered with a thick crust. They resemble rupia very closely, only they are more widely disseminated. The third is one of the most formidable manifestations of the disease and is always accompanied with profound cachexia. Rounded tubercles form, of a dark-red color, slightly elevated and firmly imbedded in the skin. A blackish slough forms in the center of each tubercle, which when cast off leaves a cup-shaped depression looking not unlike an inverted rupia crust. The ulcer is deep and foul, and secretes a fetid, ichorous pus.

Involvement of the Nails.—A papular infiltration not infrequently attacks the matrix of the finger or toe-nails. The nails themselves become brittle and dry and break into splinters as it were. This syphilitic onychia and paronychia is most rebellious and may persist so long that the shape of the nail becomes distorted.

Alopecia.—A very early and nearly always present symptom in secondary syphilis is loss of hair or alopecia. It is most noticeable on the scalp and may consist in a general thinning or it may occur

in patches. Sometimes there is complete loss of hair over the entire body. Such cases are rare. As a rule, a general thinning of the hairy parts such as the eyebrows, beard, axilla, chest and pubes aside from the scalp is all that is observed.

The toxemia of active syphilis, such as it is in the secondary stage, may produce a wide variety of symptoms. As a rule, there is no difficulty in recognizing them as such because of the history of the recent infection and because of lesions which indicate beyond doubt the presence of the disease. I refer to the more indeterminate symptoms such as acute epididymitis or orchitis, nocturnal headache and synovitis of one or more joints. This synovitis occurring in secondary syphilis is not attended with redness or tenderness of the skin over the joint. The effusion may begin slowly and painlessly or it may be sudden in its appearance. There is no tendency to go on to suppuration and under treatment the effusion soon subsides, but sometimes leaves a thickening of the synovial membrane which persists for a long time. The knee is the joint most frequently affected. Plastic iritis is a not infrequent secondary symptom. So also is choroiditis. These ocular lesions may be concomitant with the appearance of the skin eruption. Both eyes may be affected together, or each eye successively. The eyeball is injected, photophobia, lacrimation, impairment of vision and pain are present. In spite of treatment relapses are frequent.

Bone Lesions.—Contrary to the general opinion there may be early secondary bone lesions. The bones of the cranium, the sternum, ribs, clavicles and tibiæ are those most frequently affected. These secondary bone lesions are usually confined to the periosteal covering and consist in round, smooth swellings which later may become eburnated and thus cause an increase in the size of the bone. This periostitis is the cause of the nocturnal pains so often complained of in the early stage of the disease. Rheumatoid pains of the large joints and of the muscles, always worse at night and sometimes extremely severe, are not infrequent. Cardiac complications, however, are extremely rare, although I believe that syphilitic endocarditis can and does occur in the secondary stage. Among the other manifestations that may be present in secondary syphilis are jaundice and albuminuria, indicating acute disease of the liver and kidneys.

Nervous System.—That syphilis of the nervous system occurs late in the disease is the opinion held by many; but those who come much in contact with syphilis in its florid stage know that this is incorrect. Syphilitic nerve lesions in the secondary stage do not produce the degenerative changes seen in the tertiary stage as exemplified by tabes and paresis; they are more ephemeral. They appear as active exudates, partaking of the character of exanthemata of

the meninges as it were rather than as deep-seated and destructive processes. In fact it is within the first three years of the infection, which is the time covering the secondary stage, as pointed out by Naunyn and Patrick, that involvement of the nervous system is most apt to occur. Recent research has shown undubitably that nervous syphilis originates at the time of the general infection. This is proved by the fact that from 25 to 35 per cent of syphilitics examined for such have shown positive findings in the cerebrospinal fluid within a year of the appearance of the chancre. It is also true, however, that many of these cases are symptomatic or are cured, either spontaneously or by the ordinary treatment, as only a small proportion of them develop symptoms then or later.

One of the earliest symptoms indicating that the disease has attacked the nervous system is headache. It may be, and not infrequently is, coincident with the appearance of the rash. It is generally worse at night and is not, as a rule, referred to any particular part of the head. It is made worse by mental and bodily activity, but has frequently periods of remission, during which it is entirely absent. It may be the first and only symptom of involvement of the nervous system for many years. The cause of this headache is a syphilitic meningitis, either of the base or of the convexity and it should always be regarded as a precursor of some graver lesion. It is wise, therefore, in cases of cephalagia occurring early in the disease to make a lumbar puncture for the purpose of making a study of the cerebrospinal fluid.

Neurasthenia.—Neurasthenia is not infrequently present in secondary syphilis. It is nearly always accompanied with a certain degree of failure of the bodily health. For an individual who has not shown a neuropathic tendency previously and who has no apparent reason (except syphilis) for becoming so, this condition usually indicates some organic disease, or it may be due to blood changes—the result of the toxemia of the disease. The last is, in my opinion, the most frequent cause. In some instances there may be psychic disturbances of a depressive type, or this neurasthenia may be prodromal to apoplexy. The seizure in these cases differs in no way from apoplexy resulting from other causes—only the patient is apt to be very much younger than is usual when syphilis is not the predisposing cause. The apoplexy occurring in secondary syphilis is rarely, if ever fatal. Loss of consciousness, as a rule, does not occur; although the "stroke" may result in hemiplegia, monoplegia, or some disorder of speech, hearing or vision. Also, these paralyses in secondary syphilis in a majority of instances make a complete recovery. These paralyses are among the most common manifestations of early nervous syphilis. They are usually

preceded by the neurasthenic condition just described, but it must be remembered that in fully one-third of them they occur suddenly and without warning.

In secondary syphilis the nerve trunks may be attacked in the form of neuralgia—not as a neuritis, which is a neural degeneration in the tertiary stage. The sciatic nerve and the facial nerve are those most frequently affected.

In the early months of syphilis, especially in weak, underfed individuals, males more frequently than females, there is sometimes observed a condition that may be likened to a "walking typhoid" state. This condition may also be accentuated by malaria or tuberculosis or from the physical and mental exhaustion arising from alcoholic or sexual excesses. It is much more severe than the general malaise usually present at the beginning of the syphilitic toxemia. This extreme weakness frequently develops into prostration with a mild but continuous fever, frontal headache and a rapid pulse. There may be anorexia and constipation. The senses are torpid and somnolent and with this there is sometimes a mild delirium. Although seemingly serious, death never occurs, and under proper treatment the patient, after a prolonged convalescence, is restored to health. It is these cases that are affected more or less frequently with involvement of the nervous system in the early secondary stage of the disease.

The symptoms of secondary syphilis are those which occur within one or two years of the appearance of the chancre. It is, therefore, during this phase that it may be classed as an active exanthema. After the second or third year there is usually a period of quiescence which may last for one or two years or as long as thirty or forty years or even longer. These sequelæ, coming after the exanthematous stage, constitute the tertiary stage of syphilis. They differ considerably in their manifestations, clinically and pathologically, from those of the secondary stage. It is also well to remember that the secondary stage may be skipped entirely and no evidences of the infection may appear until some tertiary manifestation occurs many years after the primary lesion.

CHAPTER IX.

EARLY SYPHILITIC DERMATOSES.

The dermatoses of syphilis, as is natural to be supposed, were the first of the lesions of the disease to be described. For that reason it has been, and is yet, included in the category of dermatoses. This is true, however, only to a limited extent. The dermatologic manifestations of the disease are only a passing and comparatively benign expression of the dyscrasia. Just as much—I might say more so—is it a visceropathy, a neuropathy, a psychopathy. Syphilis can be approached from the standpoint of the internist, the neurologist, and the psychiatrist just as well as it can be from the standpoint of the dermatologist. In fact, it seems to me that it bids fair to pass out of the hands of the dermatologist into the hands of the internist who specializes in syphilis in all of its phases—the syphilologist. To him it rightly belongs. Syphilis is no longer to be considered an appendage to dermatology. The syphilologist and the dermatologist are becoming separate and distinct, as they should be. It is from that standpoint that this book has been written; the future will, I am sure, justify this.

In ancient times the distinction between skin lesions, such as we recognize today, was unknown. It was the fashion for the physicians of the time to classify all cutaneous eruptions that were chronic under the single generic term of leprosy. It was not until the pandemic of 1493 that the cutaneous lesions of syphilis were recognized as such, and Gaspard Torelli distinguished between the lesions that were moist and the lesions that were dry—a distinction, which is continued to this day. The work of von Plenck, Willan, and Bateman, and Alibert—the same "jolly old Baron Alibert" of Oliver Wendell Holmes, the first to use the word *syphilides* in describing syphilitic cutaneous lesions—established modern syphilitic dermatology.

Types of Cutaneous Lesions.—The cutaneous lesions of syphilis can, like the Gaul of Cæsar's time, be divided into three parts. To these three parts, or rather forms or types, to use words more fitting to pathology than to history, can be added a fourth, if we include the gumma, which strictly speaking is not necessarily a cutaneous lesion. These three types of cutaneous syphilis are the macule, the papule and the tubercle. All other lesions are modifications of

these three, usually because of their anatomic situation or from pyogenic infection or because two of these types of lesions combine to form a mixed or hybrid type. The cutaneous lesions of syphilis can also be divided into those which appear in the secondary stage—the early lesions, and those which appear in the tertiary stage—the late lesions. This division is the one I have elected to follow here in describing the dermatoses of syphilis. For, while it is undoubtedly true that the skin lesions of syphilis not infrequently display considerable irregularity in the time of their appearance—that is, secondary lesions may appear in the tertiary stage and tertiary lesions may appear in the secondary stage—yet it cannot be denied that in the main they follow a definite chronology in so far as the pathology of the lesions of the two stages or periods of the disease is concerned. By that I mean that the characteristic lesions of the secondary stage and of the tertiary stage are distinct and separate in their pathology and appearance.

The cutaneous lesions of the secondary stage can also be divided into early secondary and late secondary lesions. The early secondary lesions are the simple forms and the late secondary lesions the complex forms. The simple forms are the unmodified original lesions; whereas the complex forms are a combination of two simple forms or simple or combined forms modified by pyogenic infection. Thus, we have the terms pustular, crustaceous, ulcerative, squamous, maculo-papular, pigmented, serpiginous, circinate, corymbiform as descriptive of these forms.

During the first year of the disease, and especially the first half of it, we encounter the macule, the papule and the tubercle, which, as a rule, are widely spread over the body. Any one of these lesions may constitute the eruption, but it is characteristic of syphilis for the eruption to be polymorphic, that is, for the different lesions—macules, papules, tubercles—to exist simultaneously. This does not always obtain however—the lesions may be wholly macular, or wholly papular or wholly tubercular—the last being uncommon. Usually the macule and the papule are seen together, with one or the other predominating.

The dermatoses of early syphilis are almost invariably symmetrical and generalized, that is, they are equally present all over the body, which is in marked contrast to the strictly localized processes of the tertiary stage. While not infrequently the face is spared, this does not always follow. Occasionally the eruptions of the secondary stage are seen on the palms and soles, but, as a rule, these parts are not affected until the tertiary stage. The cutaneous eruptions of early syphilis, in addition to being symmetrical, seem also to follow the texture of the skin and the fine capillaries, and thus show a more or less linear tendency even when

widespread and numerous. This tendency can best be observed by examining the eruption as it appears on the back. There is no pain, burning or itching associated with the eruptions of secondary syphilis. When the eruption first appears it may at times be accompanied with a slight pruriginous feeling, but this soon passes away. In condylomata about the anus and of the genitals there may be itching and burning and at times these lesions are painful. They also frequently give rise to a characteristic disgusting odor. Mucous patches in the mouth and throat are sometimes painful but never very much so. This is in contradistinction to the excruciating pain of tuberculous ulcers. A peculiar feature of syphilitic eruptions of the secondary stage is that they appear more pronounced and distinct when viewed at a distance than when examined close by. They are also more pronounced immediately after a hot bath; especially is this true of the macular eruption, which not infrequently is discovered by the patient in this way.

Macular Eruption.—The macular is the most frequent of the secondary eruptions of syphilis. One-half of the early secondary eruptions are of this type. It is seen mostly on the trunk and limbs; it usually spares the face. The macular eruption is also known as roseola, or the roseolous eruption, because of its bright red appearance. Not infrequently, however, the roseola is very pale and hardly noticeable, and when so it is apt to be most ephemeral, disappearing in a few days and leaving no trace, so that the patient is totally unaware of its having been present. If the lesions persist they become darker—this deepening in color being more noticeable in the larger macules than in the smaller ones.

Unless the chancre has been diagnosed as such and treatment instituted at once the macular eruption usually appears within six weeks. It may appear earlier than this and sometimes it is delayed for three or four months. A delay of this length in its appearance, however, is extremely rare. The eruption gives the skin a mottled appearance, the lesions themselves being usually darker in the center and fading toward the periphery, so that the eruption is frequently vague and indistinct in so far as detecting definite macules is concerned. Not infrequently the erythematous mottling caused by the exanthema can hardly be distinguished from the normal mottling of the skin due to exposure to the air. It is these cases, I may say, that frequently show with more distinctness after a warm bath. Not infrequently the lesions show a tendency to a circinate arrangement. The macules are never elevated. Although Bassereau has stated that sometimes they are slightly elevated, I have never been able to observe this. While usually sparing the face, if present thereon, they are most marked on the forehead and chin. A macular eruption never desquamates.

Rarely it is followed by pigmentation, which, however, is not permanent. It follows with fidelity the site of the lesions and in consequence is more or less reticulated. This pigmentary reticulation—the "syphilitic collar" as it is called, is usually seen about the neck or the upper and anterior aspect of the chest. It is essentially a secondary dyschromia and represents a sequela or consequence of the syphilitic maculation.

Occasionally a roseola recurs after having disappeared. This usually happens during the first year of the disease and in cases that have been insufficiently treated. When this occurs the lesions show a tendency to assume crescentic or circular forms. The roseola of syphilis is to be distinguished from pityriasis rubra of Gibert by the absolute absence of desquamation. It is to be distinguished from the balsamic roseolas by its less intense color and the absence of pruritus. From the roseola of leprosy and of mycosis fungoides it is to be distinguished with difficulty. These diseases, however, are extremely rare in this country and are also accompanied by other characteristic signs. The roseola following the ingestion of antipyrin shows a close resemblance to the roseola of syphilis; but the history of having taken this drug and the fact that the eruption rarely lasts longer than a week and the absence of a positive Wassermann reaction and of other signs of syphilis present in the secondary stage, will distinguish it from the syphilitic eruption. The macules sometimes present in scabies or pediculosis may cause confusion in the diagnosis; but the itching and the presence of the *acarus scabiei*, or itch mite, or of the *pediculus corporis*, or louse, should enable a diagnosis to be made.

Papular Eruption.—Next in frequency to the macular eruption is the papular eruption in secondary syphilis. The papule differs from the macule in that it presents greater clinical variation, is distinctly circumscribed and usually indicates a more severe infection. The eruption is usually abundant and widespread and is more frequently observed on the face than the roseola. It is more frequently accompanied by alopecia and by mucous patches—which are nothing more than papules situated on a mucous surface—than is the macular eruption. Papules are classified according to their size, into miliary or follicular—because they always surround a hair follicle—lenticular, and large or discoid. They are round, slightly elevated, circumscribed infiltrations of the skin. They are bright red in color and present an appearance as if the patient's body had been copiously sprinkled with red-lead paint. If treated they disappear promptly—within a week or ten days or even less; but if untreated they often persist for several months. Whether treated or not they frequently leave reddish or yellowish pigmented spots which are sometimes difficult to clear up. These

are the *syphilides nigricantes* of Fournier. I have found that they can be made to disappear by anointing them daily with a 2 per cent ammoniated mercury ointment. The papule desquamates; the macule does not. This desquamation begins as a fine scale in the center which, when it falls off, leaves a number of minute

FIG. 17.—Papular syphiloderm. (Courtesy of Dr. M. B. Parounagian.)

scales at the periphery of the lesion. This scaly border is known as Biett's collar. The peripheral scaling does not always occur, and it is by no means pathognomonic of syphilitic papules.

The miliary papule is the smallest of the papules and it always surrounds a hair follicle. It is conical rather than flat and varies from a pinhead to several times that size. Often a minute scale

or a pustule may be found on the top. It is widespread and usually is arranged in a circinate grouping. The extensor surfaces of the arms and legs and the back and sides of the chest show the greatest number of the lesions. Sometimes, but not often, they are seen on the face. A miliary papular eruption develops rapidly and is rather slow in disappearing unless influenced by treatment. Minute pigmented spots or else minute scars, if there has been pustulation, are to be observed in many instances after the eruption has passed. Miliary papules are sometimes mistaken for lichen planus, but in syphilitic papules there are not the whitish or grayish striæ which may be observed on the papules of lichen. The papules of lichen differ in color from those of syphilis; whereas syphilitic papules are bright red, those of lichen are more of a lilac color. Pruritus may or may not be present in lichen; if present, it is apt to be extreme; it is never present in syphilitic papules. While buccal lichen is sometimes present and may be mistaken for mucous patches, it is to be remembered that buccal lichen gives rise to no discomfort in the mouth which certainly cannot be said of mucous patches. If the lesions are syphilitic there will always be found a general glandular enlargement, possibly the scar of a recently healed chancre and usually other signs of syphilis, including always a positive Wassermann reaction.

The lenticular papule, as its descriptive prefix implies, is about the size of a lentil, that is somewhat less than 1 cc in diameter. It is much more frequently encountered than the miliary papule and, next to the roseola, is the most frequent eruption of secondary syphilis. They are usually widely disseminated and are prone to appear on the face as well as the rest of the body. These lesions are almost invariably discrete but frequently are more or less grouped. This grouping may assume annular or circinate configuration. Scaling is nearly always the rule, and it is in this type of papules that the so-called collar of Biett is most frequently observed. In some instances, frequently on the face, the grouping may assume a corymbose arrangement—so named because of the fancied resemblance to a bunch of grapes—which may be mistaken for lupus erythematosus. The corymbiform papular eruption usually consists of a single large papule around which are a number of smaller lenticular papules. The smaller papules may form a complete ring around the larger papule with an intervening area of healthy skin, or the smaller papules may be grouped irregularly around the larger papule.

While sometimes mistaken for lupus erythematosus, there are certain differences between the two processes which will enable a diagnosis to be made without difficulty. Lupus erythematosus is much more sharply defined than the corymbiform papular syphilide.

In lupus erythematosus the follicles are enlarged and filled with sebaceous material that forms minute plugs; these sebaceous follicular plugs are never found in papular syphilides. Lupus erythematosus is of slow development, whereas the papular eruption develops very rapidly.

The large, or discoid, also called mummular papule is sometimes seen as a generalized eruption in secondary syphilis. It is not often the first eruption; but it not infrequently follows five or six months after a previous macular eruption, in cases that have not had sufficient treatment. It is frequently seen on the face and about the orifices of the body, such as the mouth and anus; also the vagina in females and the scrotum and penis in males. These large papules when so situated are frequently transformed into condylomata lata. On the cutaneous surface they soon become scaly, or in some instances, especially if allowed to persist, they may ulcerate. When they disappear they leave pigmented areas and in those instances where there has been ulceration, atrophic scars may remain.

Palmar and Plantar Papules.—Papules sometimes occur on the palms and soles. They are not frequent and are usually those of the larger size. When so occurring they differ somewhat from those occurring elsewhere because of the thickness of the horny epidermis. In appearance they are of a dark red color and are deeply imbedded in the skin; they are not elevated but rather are depressed and are covered with scales. If the papules are of the lenticular variety they show a tendency to form in circles. The scales superimposed upon the lesions give them a yellowish-gray color, but when removed the underlying patch is found to be the characteristic red ham color. If the lesions are numerous or large the infiltration of the skin caused thereby renders it inelastic and more or less brittle and, in consequence, fissures are apt to form. These palmar and plantar papules are extremely resistant to treatment and not infrequently persist long after all other cutaneous lesions have disappeared. They are sometimes mistaken for eczema but differ in being more sharply defined, their circinate contour and their darker red color are also characteristic.

When papules occur on opposing cutaneous surfaces which are subjected to heat and moisture, such as the scrotum, about the anus, the mammary folds, the groins when the abdomen is pendulous and sometimes in the axilla and between the toes, the maceration of the epidermis arising therefrom causes these otherwise dry papules to be transformed into moist papules. The continued irritation causes the epidemic papillæ to become hypertrophic, so that they quickly assume a flat, wart-like appearance. These lesions, according as they develop from a lenticular or large papule vary

in size from a pea to a lima bean or even larger. They are slightly raised above the surrounding skin, are sharply demarcated, and are covered with a seropurulent secretion of most offensive odor.

Mucous Patches.—Papules occur with great frequency on the mucous surfaces in the early stage of syphilis. These lesions are known as mucous patches and are among the most characteristic and pathognomonic lesions of the disease. They are highly infectious and from them the disease is most frequently contracted. The mouth and tongue, the throat, and the genitals of both sexes are where they are most frequently found. The mucous patch occurs as a red and glistening, sharply circumscribed surface, slightly depressed in the center and with the edges, therefore, slightly raised. It is not indurated and may be covered with a yellowish pellicle or the pellicle may be whitish, not unlike that caused by painting the mucous membrane with a strong solution of silver nitrate. The mucous membrane surrounding the lesion may be slightly edematous, but this is not always so. Mucous patches are usually oval in shape, but where several coalesce their shape may be irregular. They are only slightly painful but their presence in the mouth frequently gives rise to considerable discomfort. When occurring on the tonsils or the larynx or pharynx they frequently give rise to a marked angina. The voice also may become husky and hoarse—the *vox syphilitica* of the older writers.

Treatment of Mucous Patches.—It may not be out of place here to discuss the local treatment of mucous patches and then to discuss the lesions occurring in the mouth—such as mercurial stomatitis—that sometimes follow and which are not infrequently confused with mucous patches when they are present in the buccal cavity. If mercury is to follow arsphenamine—and in my opinion it always should—the teeth should be attended to before this drug is given. During its administration, in no matter what form, a mouth wash of potassium chlorate should be used daily. I have found the following to be a useful formula for this purpose:

℞—Potassii chloratis . . . . . 6 gms.
Tincturæ gentianæ . . . . . 8 cc
Aquæ menthæ piperitæ. . . . . q.s. ad 240 "
Misce.
Sig.—Use as a mouth wash three or four times a day.
Instead of this, potassium chlorate lozenges may be used, one to be dissolved in the mouth three or four times a day.

The treatment of the mucous patches consists in touching them daily with a cotton applicator dipped in a 4 per cent solution of nitrate of silver. I do not believe in applying to the lesions caustics such as chromic acid or acid nitrate of mercury. Other than the daily applications of the nitrate of silver and rinsing the mouth

with some mild antiseptic solution such as the official liquor antisepticus no local treatment is necessary. Mucous patches occurring about the anus or genitals or in cutaneous folds should be treated with the silver nitrate solution, or else dusted once or twice a day with powdered calomel.

Mercurial stomatitis manifests itself as superficial ulcerations covered with a whitish pellicle around the neck of the last molar tooth, or the necks of the lower incisors, or on the borders of the tongue. It is always accompanied with more or less salivation and a characteristic disgusting fetor of the breath. The stomatitis caused by mercury is at times most severe; gangrene of the buccal mucous membrane and gingivitis from which the teeth may fall out sometimes occurs. It is a condition that is fortunately becoming rare, because mercury is no longer administered in the massive and long-continued doses of former times. The treatment of this condition will be found in the chapter on the General Treatment of Syphilis and, therefore, I will not discuss it here.

Maculo-papular Eruption.—Not infrequently the generalized infection of syphilis is heralded by an eruption that partakes of the character of both macules and papules. This maculo-papular eruption is, as its name implies, an eruption of papules interspersed upon a generalized macular eruption. Each papule, therefore, is surrounded by a macular halo and the generalized erythema is spotted in consequence by small patches of deeper red papules. When well developed the eruption bears a somewhat close resemblance to urticaria.

Tubercular Eruption.—The tubercular or nodular syphilide is in reality a small cutaneous gumma and as such is to be included in the tertiary rather than in the secondary eruptions of the disease. However, as it forms one of the three main divisions of syphilitic skin eruptions, and also as it occasionally appears as a generalized eruption in the secondary stage, it will be described here in so far as it is a manifestation of early cutaneous syphilis.

The syphilitic tubercle appears as a circumscribed and imbedded infiltration with a conical or rounded top projecting from the cutaneous surface. It is of a dark red color and may have on its summit a scale or it may pustulate. It is rarely diffused and when it is it denotes a most severe and often prostrating infection. These tubercles show a decided predilection for the face, especially the nose and cheeks, and when so occurring they are also usually present on other parts of the body as well. In the secondary stage they rarely ulcerate, but in the tertiary stage they very frequently do, and this phase of their pathologic activity will be discussed in the chapter on the Late Syphilitic Dermatoses.

It is usually stated that a syphilitic eruption of the herpetiform

type is rare; in my opinion, however, it is not as rare as is usually supposed. These lesions are really minute papulo-vesicles which in many instances are changed into papulo-pustules. The eruption, although widespread, is nearly always discrete and shows a decided tendency to group in circles or segments of a circle. This syphilitic herpetiform eruption is to be differentiated from a follicular papular eruption which in a way is a secondary consideration, but more particularly is it to be differentiated from keratosis pilaris, follicular eczema, pityriasis rubra pilaris and acne. Keratosis pilaris is nearly always localized about the eyebrows and forehead and on the underside of the jaws. It is often followed by a loss of hair of the parts affected—the eyebrows and beard, which also show minute scars. Herpetiform syphilides are not confined to any particular part of the body—in fact, the face is usually spared, nor is the eruption followed by scarring; it disappears and leaves no trace. Follicular eczema is attended with itching; the syphilitic eruption is not. Pityriasis rubra pilaris begins in spots which extend peripherally. The lesions are sharply defined and sometimes are covered with fatty yellowish scales; or again, there is sometimes a serous oozing which later dries and forms thin crusts, there is also pruritus. Herpetiform syphilides appear as a more or less generalized eruption and the scales, if present, are exceedingly minute and dust-like; there is no weeping from the lesions and they never itch. The various forms of acne can usually be distinguished from a syphilitic herpetiform eruption in that they are of slower evolution and are nearly always accompanied by comedones and are frequently pustular. In all of these conditions a Wassermann reaction will quickly clear any doubt that may exist.

Pustular Eruption.—An eruption that is pustular from the onset is rare in syphilis. Nearly all pustules develop from papules. There is first a serous exudate under the epidermis in the center of the papule which quickly becomes purulent. Since the pustules form from papules they may be follicular, that is, they may arise from the peripilar papules or they may arise from a lenticular or from a large papule. The pus in these papulo-pustules soon desiccates into a yellowish-brown crust which soon falls off showing a small ulceration or cicatrix beneath. When a large papule is transformed into a pustule, which then presents as a somewhat flaccid pustular bleb or bulla, it is known as syphilitic ecthyma or as an ecthymatous syphilide. These particular lesions are extremely rare in early syphilis, that is, within the first year of the disease, but they sometimes occur in the latter part of the secondary stage in those who are cachectic from any cause. In the tertiary stage when syphilitic ecthyma is most likely to occur it is frequently the beginning of rupia.

A papulo-pustular eruption that comes on acutely and which is generalized may simulate variola or small-pox very closely. Not only does it do so in the eruption but in the character of the fever and the backache as well. A syphilitic pustular eruption, however, is to be distinguished from that of variola in that no matter how rapidly it develops—for syphilis—it never develops as rapidly as the eruption of variola. Neither does the syphilitic eruption itch when undergoing resolution as does the eruption of variola. When secondary syphilis manifests itself in this manner it may well be looked upon as malignant and fortunately is most rare.

Pigmentation.—All syphilitic lesions are likely to be followed by more or less pigmentation. The pigmentation that frequently follows an intense macular eruption and that is sometimes seen about the neck and the upper part of the chest I have already mentioned. In some instances, however, instead of pigmentation there occur areas in which pigmentation is almost or entirely absent—a syphilitic vitiligo as it were. This hypochromia usually follows upon the site of a former cutaneous lesion, but in some instances, at least, it occurs in the absence of such and as a primary dyschromia.

Urticaria.—A dermatosis that is met with comparative frequency in secondary syphilis is urticaria. In 100 cases studied by Hazen he obtained a positive Wassermann reaction in 33. Hazen states that it is more frequent in negroes than in whites. However this may be, in all cases of chronic or persistently relapsing urticaria, syphilis should be suspected.

The secondary lesions in those rare cases, which are generally termed malignant, may become hemorrhagic. It is to be noted in this connection, however, that purpura or hemorrhagic extravasations into the skin sometimes follow long-continued and excessive doses of potassium iodide.

It must not be forgotten that cutaneous syphilis in its early as well as in its late manifestations may occur in combination with other skin diseases, these latter existing perhaps long before the syphilitic infection was acquired. In such instances the pre-existing dermatosis is almost invariably unfavorably influenced. It must also be remembered that syphilis can simulate any known skin disease—and simulate so closely that sometimes it is impossible to clinically differentiate whether a given dermatosis is syphilitic or not. As may be supposed, the dermatoses of early syphilis are more likely to be mistaken for those dermatoses due to other causes that run a more or less acute course, although in some instances this is not so, as exemplified by lupus erythematosus and vitiligo. A brief résumé, therefore, of those dermatoses with which early syphilitic dermatoses may sometimes be confused will not be out of place.

Dermatoses Resembling the Macular Eruption.—The macular eruption, or roseola, of syphilis is to be distinguished from pityriasis rosea, the roseolas of various drugs, such as balsam copaiba, and

FIG. 18.—Papulo-squamous syphilide (psoriasiform). (Courtesy of Dr. M. B. Parounagian.)

antipyrin, the erythemas due to various causes, including anaphylaxis, the roseola of leprosy and of mycosis fungoides — the last two being extremely rare.

Dermatoses Resembling Papular Eruption.—The papular eruption of syphilis may at times be mistaken for lichen planus, psoriasis, the diffuse and circumscribed prurigos and eczema.

FIG. 19.—Pustular syphiloderm. (Courtesy of Dr. M. B. Parounagian.)

Dermatoses Resembling Tubercular Eruption.—Syphilitic tubercles may be mistaken for the tubercles of leprosy or for disseminated miliary lupoids. Of these the first is rarely encountered in this country; the second is sometimes extremely difficult to diagnosis.

Dermatoses Resembling Pustular Eruption.—Syphilitic pustules may be mistaken for small-pox—rarely, for chicken-pox; they may also be confused with acne, with impetigo and with ecthyma, with glanders and with the various mycoses.

Dermatoses Resembling the Pigmentation of Syphilis.—The pigmented syphilides may be mistaken for the various dyschromias, such as chloasma, leukoderma and vitiligo.

Numerous as these analogies may be however, if searched for carefully there will nearly always be found some differences in the

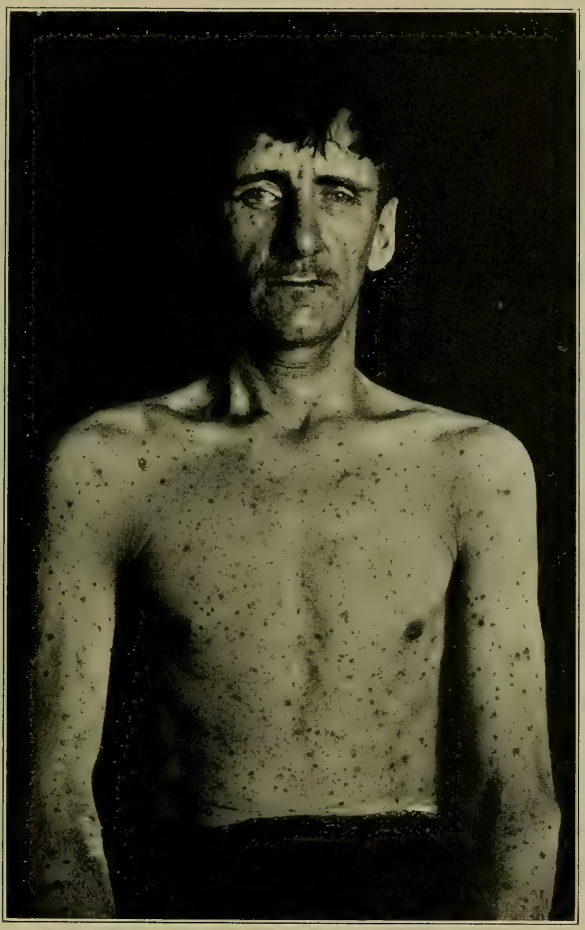


FIG. 20.—Varioliform syphilide. (Courtesy of Dr. M. B. Parounagian.)

appearance of the lesions or confirmatory evidence of some other kind that will tell either for or against syphilis. Last, but not least, the physician always has two strong staffs to lean on—the Wassermann reaction and the therapeutic test; and in those cases in which the clinical manifestations are confusing or cannot be

determined because of inexperience—these two will always be the signs infallible of syphilis or not.

Cutaneous eruptions are frequent and characteristic in early congenital syphilis. So frequent and characteristic are they in fact that a diagnosis can in nearly every instance be made by them alone.

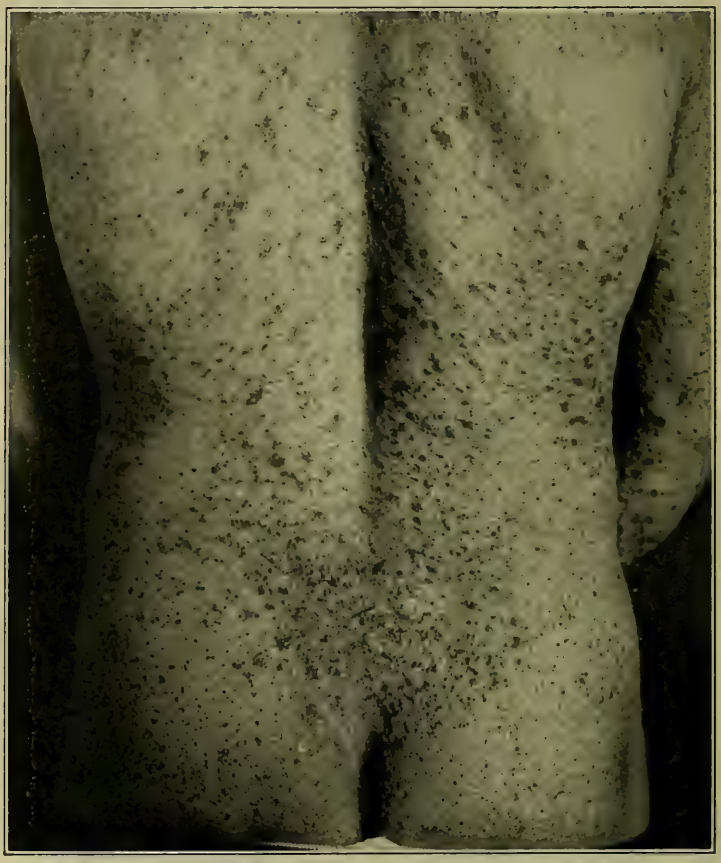


Fig. 21.—Follicular syphiloderm. (Courtesy of Dr. M. B. Parounagian.)

Eruption in Congenital Syphilis.—Only rarely—very rarely—is a congenitally syphilitic infant born with an eruption. While it undoubtedly occurs, and in some text-books the reader is led to believe that it is the usual occurrence, a rash of any kind in a newborn infant is most unusual. The eruption of congenital syphilis usually appears in from two to eight weeks after birth; it is some-

times deferred for another five or six weeks. Findlay reports a case deferred until the fourth month and another at the ninth month, but such instances are so rarely encountered that they may be very properly discounted unless there have been other evidences of the disease previously existing. The eruption may be macular, papular, or pustular, the last being vesicular before it becomes pustular—*phemphigus syphiliticus.*

Macular Eruption in Congenital Syphilis.—As in acquired syphilis the macular eruption is the one most frequently observed in the congenital form of the disease. This maculation appears as a diffuse erythema, especially pronounced about the buttocks and genitals, although it is frequently diffused over the entire body. The color of the macules varies from a yellowish-red to a deep copper color. When it first appears the rash may be localized about the parts already named and instead of being diffused is more or less circumscribed. It is not until later that these circumscribed patches coalesce and spread peripherally. On the legs the eruption is to be found mostly on the flexor and inner surfaces rather than on the extensor and outer surfaces. Except in the folds of the buttocks the eruption is dry and scaly—this scaliness being especially characteristic. In the fold between the buttocks and about the genitals the eruption takes on a moist appearance and scattered over the surface of this moist erythema are small areas of eroded epithelium, showing as glistening spots from which serum may exude. Macules are not infrequent on the palms and soles and usually desquamate early—the desquamation beginning at the periphery of the lesions, as a rule, the macular eruption takes about a week to fully develop, and it disappears promptly under treatment.

Papular Eruption in Congenital Syphilis.—The papular eruption is sometimes the first cutaneous manifestation of congenital syphilis. In not a few instances it is present along with the macular eruption. Where the two eruptions are present at the same time the macular eruption usually predominates; the papules are scattered irregularly over the body, and are few in number, generally not more than four or five. The crescentic grouping of the papules so often seen in the acquired disease is usually absent in the congenital form. Follicular papules are rarely seen in the congenital eruption; the lenticular or large papules are those almost invariably found. The tendency to scale or desquamate is present to a marked degree in these lesions. This scaliness and peeling of the skin, occurring in the course of an eruption in an infant less than three months old, should always arouse the suspicion of congenital syphilis even in the absence of other signs of the disease.

Where papules occur between two opposing cutaneous surfaces

or at the junction of cutaneous and mucous surfaces, or wherever there is moisture and friction, they almost invariably, unless checked by treatment, develop into condylomata lata. As in the acquired disease, this is a hypertrophy of the lesion which becomes transformed thereby into a flat papillomatous excresence. Their size and shape are governed by the configuration of the parts upon which they grow; they are of a pinkish color and in weakly cachectic infants a false membrane may form which is slightly adherent and when removed leaves a raw and bleeding surface. The surface of these lesions is often fissured and ulcerated and at all times exudes a scanty, offensive secretion that is highly infectious. Condylomata lata are among the earliest lesions of congenital syphilis to appear. In infants they are mostly seen about the anus, but not infrequently occur at the angles of the mouth and when present there are almost invariably associated with mucous patches in the buccal cavity. Because of the movements of the infant's mouth and the friability of the lesions, fissures or rhagades frequently form which upon healing leave the radiating scars that are practically pathognomonic of congenital syphilis.

Pustular Eruption in Congenital Syphilis.—Pustular or pemphigoid eruptions occur early in congenital syphilis. They very frequently occur shortly after birth—sooner in most instances than the macular or papular eruptions. A pustular eruption is always indicative of a severe infection and of low bodily resistance. A very large percentage of these infants die. There are exceptions to this rule, however, as syphilitic pemphigus is sometimes seen in infants who are seemingly in fair health otherwise. The pustules that appear early are the largest, and the earlier and larger the pustules are the more grave is the prognosis. Pustules that appear after the eighth week are more apt to be smaller and fewer in number, and the disease in these instances offers a better prognosis. These pustules may be spread over the entire body, but they are usually seen mostly on the thighs, buttocks and face. They vary in size from a lentil to a bean and may be flaccid or distended with pus. These pustular syphilides may be grouped about the mouth, or they may occur in groups on other parts of the face or on the hairy scalp. Groups of pustules surrounded by a deep red infiltrative inflammation may form on the palms and soles, or at the base of the nails—usually those of the fingers—which may be destroyed thereby. Should the infant survive, the pustules after healing leave no trace.

In some few instances the vesicles do not become pustular and remain as vesicles or blebs throughout their course. This rarely happens, however, and vesicular syphilides are counted among the uncommon lesions of the disease.

In some rare instances papules may condense into tubercles

and appear as sharply defined tumors in the skin somewhat less than 1 cm. in diameter. They are usually few in number and are usually associated with papules. They may disappear and leave no trace or they may break down and form ulcers which are extremely obstinate in healing.

During the first year of life and sometimes later the integument of the infant may be attacked with furunculosis. These furuncles of congenital syphilis differ somewhat, however, from the ordinary boils of infancy. They form slowly, without showing signs of inflammation, as small nodules in the corium. They gradually increase in size until they are as large as a nutmeg. A superficial ulceration occurs on the top and a slough forms, which when it comes away leaves a deep cavity in the skin with unhealthy walls and surrounded by a dark red areola. If numerous they are usually symmetrically arranged; if few in number their disposition is irregular. They discharge a scanty, sanious pus and are slow to heal even under vigorous constitutional treatment.

Mucous Patches in Congenital Syphilis.—Mucous patches occur in early congenital syphilis with the same frequency that they occur in the acquired form. Clinically and pathologically they do not differ from the same lesions seen in adults.

The cutaneous lesions of early congenital syphilis are, on the whole, more characteristic and therefore easier to diagnose than those of the acquired disease. Eruptive diseases are comparatively infrequent in the first six months of life; there are, however, some affections of the skin that are frequently met with in early infancy which may give rise to some confusion in diagnosing between them and the syphilitic exanthemata. Of these the most difficult to diagnose is intertrigo or gluteal erythema of the newborn. It is a condition that is frequently met with and if at all severe, or if it does not rapidly clear up, it very closely simulates a congenital syphilitic dermatosis. In fact, in many instances clinical differentiation is impossible and resort must be had to the Wassermann reaction or the finding of the Treponema pallidum in the lesions. There must be no resort to the therapeutic test in these cases to clear up the diagnosis—arsenic or mercury must not be given until the diagnosis has been definitely established by the measures named. Macular syphilides attended with extreme desquamation may resemble somewhat a mild form of ichthyosis but the non-occlusion of the nostrils or the ears by the excessive production of epithelial cells, the absence of ectropion and the absence of other deformities of the mouth and anal orifice due to contractions of the skin, and the absence of imperfectly developed nails and hair are indicative of syphilis rather than ichthyosis. The Wassermann reaction, however, will confirm the diagnosis one way or the other.

Miliaria rubra, or sweat rash, may be mistaken for a syphilitic eruption in an infant. Miliaria rubra is usually observed upon the cheeks and neck and is usually more pronounced or it may be confined wholly to the side upon which the infant sleeps. Small papules appear about the sweat glands which may be topped with minute vesicles. If the lesions are not syphilitic they will promptly disappear by clothing the infant more lightly, changing the side upon which it sleeps and dusting the lesions with a powder composed of equal parts of boric acid and starch. Eczema may sometimes be mistaken for a syphilitic eruption but if it is remembered that syphilitic eruptions never itch the diagnosis can be easily made. Herpetiform syphilides are so extremely rare that they need hardly be considered; herpes febrilis is also equally rare in infants less than a year old. Syphilitic pustular eruptions developing shortly after birth may be confused with non-specific bullous impetigoes. It may be extremely difficult to diagnose between these two dermatoses. The non-specific varieties, however, never develop on the palmar or plantar surfaces and they are autoinoculable; these two distinguishing features are sufficient to differentiate them from those due to syphilis. Non-specific furunculosis consists of true boils rather than of nodules that later become necrotic as is the case in syphilitic furunculosis. The discharge from the non-specific furuncles is frankly pustular, whereas the discharge from the furuncles of syphilitic origin is ichorous.

In concluding this chapter I wish to emphasize the fact that in not a few instances clinical differentiation between syphilitic and non-syphilitic skin eruptions occurring in infants is a matter of extreme difficulty. For that reason, when the issue involved is considered, the diagnosis of the existence or non-existence of syphilis should not be lightly or hastily made. If there is any doubt a Wassermann test of the blood should be made.

CHAPTER X.

EARLY NERVOUS SYPHILIS.

That syphilis of the nervous system is a late manifestation of the disease is the opinion held by many; but those who come much in contact with the disease know that this is incorrect. Syphilis can and does attack the nervous system in the earliest stages of its invasion. In fact, it is within the first three years of infection, as pointed out by Naunyn and Patrick, that nervous syphilis is most likely to occur. Nor is syphilitic nervous disease a rare manifestation. It is quite frequent—more so than many would suppose.

It has been recently shown that nervous syphilis undoubtedly originates at the time of the general infection, that is, simultaneously, or rather shortly after the appearance of the chancre. This is proved by the fact that from 25 to 35 per cent of syphilitics have positive findings in the spinal fluid within a year of the appearance of the chancre. While it is undeniably true that many of these are cured spontaneously as it were, or by the ordinary treatment which they receive, yet all of these are potential candidates for nervous disease, be it a transient hemiplegia or the more severe forms of nervous syphilis, such as tabes and paresis.

The phenomena observed when the treponemata prey upon the central and peripheral nerves present some of the most abstruse problems of syphilis. While many who contract syphilis are exempt from nerve involvement and show a tendency rather to the grosser lesions of the skin and bones and other viscera, yet in a large number of individuals the disease seems to single out the nerves for its most ferocious onslaught. Because of this seeming electiveness there are those who hold that the Treponemata pallida which invade the nervous system are a special strain having a predilection thereto. Others again believe that the advent of nervous syphilis is largely a question of the lack of resistance of the nerve elements themselves. If these have been weakened by excesses of any kind, or by some intercurrent disease, or if inherently weak so that they are a *locus minoris resistentiæ*, the nervous system is almost certain to be affected. This may be in the early stages of the disease, or it may be deferred for many years. I am not in accord with the theory of special strains of treponemata. It is in

my opinion entirely a question of the resisting powers of the nervous system.

Factors in Nervous Syphilis.—While syphilis is of world-wide incidence and attacks indiscriminately every race and tribe under the sun, the black and yellow races are singularly free from nervous syphilis. This is undoubtedly due to their nervous system being of a more elementary grade and therefore more resistant to disintegrating influences. It is also to be noted that age is a factor in the occurrence of nervous syphilis. The younger the syphilitic the better are his chances to escape its ravages. Syphilis acquired late in life is much more frequently complicated with nervous lesions. Paradoxical as it may seem, women, who are more highly strung and nervously unstable than men, are relatively free from nervous syphilis. It is also well to remember that nervous lesions occurring in the secondary stage of the disease are much more amenable to treatment than are tertiary lesions. This is because the secondary lesions are of an exudative character and therefore can be eliminated by therapy, while tertiary lesions are usually degenerative and destructive and unless treatment is applied before these changes have occurred the destroyed tissues cannot be replaced and the functions which they control cannot be restored.

Headache.—One of the earliest, if not the earliest, symptom of involvement of the nervous system is headache. Most French syphilologists teach that headache in secondary syphilis, unless caused by a periostitis of the cranial bones, is the result of a basal meningitis. With this opinion I am in accord. This headache, which is characteristic of syphilis, is usually coincident with the appearance of the rash or it may occur even earlier. As in most syphilitic lesions attended with pain, it is usually worse at night and is not, as a rule, referred to any particular part of the head. It is made worse by mental or bodily activity, but frequently there are periods of remission during which it is entirely absent. The cause of this headache occurring so early in the course of the disease is a syphilitic meningitis which may be of the base or of the convexity. It may also be caused by an inflammation of one of the cranial nerves in the locality of its passage through one of the bony canals. Later it may be due to a syphilitic arteritis of the cerebral arteries. This may be the first as well as the only symptom of nervous syphilis for many years, during which time the patient may seem perfectly well. But when present it should always be regarded as the precursor, perhaps many years removed, of cerebral syphilis. For that reason whenever it occurs a lumbar puncture should invariably be made and the spinal fluid examined and if the findings warrant, intraspinous therapy should be instituted at once.

Neurasthenia.—An early indication of syphilitic neurosis is neurasthenia. As in neurasthenias arising from other causes there is always a certain degree of failure of bodily health. In syphilitic neurasthenia this is, of course, due to the toxemia caused by the disease. This condition is brought out most prominently when the patient is a brain worker or is occupied as an executive. The usual symptoms of neurasthenia are present, such as inability to fix the attention, failure of memory, irritability, inability for sustained effort; and the patient is fully conscious of all of these. Associated with these mental symptoms is some disturbance of function such as dyspepsia. Under proper treatment the condition usually passes away in a short time and the patient regains his normal frame of mind.

In some instances, however, especially if the patient is addicted to alcoholic or sexual excesses, the outcome is quite different. Instead of a syphilitic toxemia with its attendant symptoms common to any other chronic toxemic condition, an acute and more or less localized exudative inflammatory process suddenly develops and the result is syphilitic apoplexy. The seizure or "stroke" in these cases differs in no way from apoplexy arising from other causes; only the patient is apt to be very much younger than when syphilis is not the predisposing cause—unless—it must always be remembered, the disease has been acquired late in life. Also this early syphilitic apoplexy is likely to be slight and is rarely if ever fatal. As a rule, the patient soon recovers, even without treatment, although some disorder of speech, hearing or vision may persist for a time. Rarely does loss of consciousness occur; although the "stroke" may result in hemiplegia, monoplegia or hemiparesis. These paralyses are among the most common manifestations of early nervous syphilis, many times occurring within six months of the initial lesion. While they are usually preceded by the neurasthenic symptoms just described they may come on gradually, often accompanied with neuralgic pains, or tingling and numbness or other disorders of sensation. When the onset is gradual complete paralysis of the part rarely occurs.

Occasionally aphasia may be an isolated symptom; so, too, may paralysis of the motor-oculi nerves. Syphilis undoubtedly has a predilection for the third cranial nerve as every syphilologist can testify. The syndrome known as Ménière's disease, in which the symptoms are sudden deafness, nausea and vomiting, tinnitus, nystagmus and vertigo, may be due to syphilitic disease of the labyrinth or to a syphilitic lesion of central origin occurring early in the course of the infection. Balzer reported a case occurring nine months after infection. Syphilis in the early stage may attack the ninth, or glossopharyngeal, nerve and cause disturbances

of taste, which may be lost (*ageusia*), or more acute than normal (*hypergeusia*), or perverted (*parageusia*).

Meningo-myelitis.—Meningo-myelitis is not, as was formerly supposed, a late manifestation of syphilis. It may occur early in the secondary stage. In 74 cases collected by Savard, the condition occurred before the end of the second year in nearly one-half of the cases. Goldflam reported a case which developed three months after infection. The symptoms in these cases are due to involvement of the roots of the spinal nerves and of the cord itself. The symptoms are parathesias, hyperesthesias, and severe neuralgic pains. Intercostal neuralgia or sciatica occurring shortly after a syphilitic infection should arouse suspicion of spinal syphilis.

Pseudo-tabes.—The term pseudo-tabes has been given by Oppenheim to a symptom complex which more or less resembles true tabes. It is due to a meningitis of the posterior roots of the spinal nerves with secondary degeneration of the posterior columns. It is essentially a manifestation of the secondary stage of the disease. The onset is usually rapid with periods of remission. The Argyll-Robertson pupil so characteristic of true tabes is, however, rarely if ever present and serves to distinguish clinically this form from the graver form of the tertiary stage. The knee-jerks are variable. They may be present, absent or exaggerated. There is rigidity and pain in the spine which radiates to the legs and arms. The Wassermann reaction of the spinal fluid is usually negative if less than 1 cc of fluid is used—much more so even than in true tabes, but the leukocyte count as would be supposed is much increased. Pseudo-tabes is quickly amenable to treatment in which respect it differs greatly from true tabes unless attacked in the early stages.

Polyneuritis.—Primary polyneuritis not infrequently occurs in the secondary stage of syphilis. Menard describes five types: motor, sensory, mixed motor and sensory, trophic, pseudo-tabetic. In the sensory type there are disturbances of sensation, particularly the peculiar disturbance known as formication, in which the patient complains of a feeling as if ants or other insects were crawling over the skin. Pain in the limbs is also a prominent symptom. In the motor type there is progressive muscular weakness which may go on to paralysis. In the trophic type, symptoms such as alopecia areata or ulcers of the hand or foot, may develop.

Spinal Syphilis.—Syphilis of the spinal cord is the most frequent form of nervous syphilis and nearly all of its lesions can and do occur early in the disease. These lesions include meningitis (pachymeningitis, leptomeningitis, meningomeningitis); also various analogous forms simulating other nervous diseases. It is well to remember that there are no characteristic symptoms of syphilis of the spinal cord; but there are certain symptoms, which if they

occur in young adults, especially males, should cause us to suspect a possible luetic infection. These are severe intercostal pain, worse at night; pain in the extremities with contractures of the muscles; incontinence or retention of urine not due to stricture or acute gonorrhea; disappearance and reappearance of the patellar reflexes.

Cerebral Syphilis.—Cerebral syphilis, as an early manifestation of the disease, is by no means uncommon. The base of the brain is more frequently attacked than the convexity. A true basilar meningitis may develop or it may take the form of vascular changes in the small nutrient vessels and the perivascular lymph spaces. In addition to the brain structure the cranial nerves may also suffer. If the lesion is focal, some one symptom will stand out to the exclusion of others, but if the process is diffuse the symptoms will be numerous. Basilar syphilis should be as much of a catchword as it were, as paresis or tabes. Cortical syphilis, syphilitic meningitis of the vertex as distinct from paresis, is also an important entity. As in the basilar form, if focal lesions occur we encounter isolated symptoms referred to the part affected. An important generalization is this—*cortical syphilis never occurs alone; there are always lesions elsewhere in the body.* Frequently there is a diffuse meningo-encephalitis which is the pathologic basis of paresis and yet the patient may not develop the latter. It is stated by Jelliffe that meningo-encephalitis may so closely simulate paresis that it is well nigh impossible to differentiate between the two.

One of the most important symptoms of cerebral syphilis, as already stated, is headache. It is, I may say, a cardinal symptom, and its presence in a syphilitic should always cause an investigation of the spinal fluid to be made. In some instances there are symptoms of increased intracranial pressure. These are choked disk, slow pulse, projectile vomiting and delirium. Strabismus and anisocoria may also be present, also facial palsies and neuralgias, if the corresponding nerves are included in the process. These symptoms may foretell either a psychosis or a suddenly appearing coma.

These desperate types of cerebral syphilis can all develop within a short time of infection. In this respect they contrast greatly with paresis which does not appear for many years after the initial lesion and is the slowest developing disease known. As a rule, early brain syphilis responds readily to proper treatment. It is the neglected cases that fare badly. In passing I desire to say that there should be no timidity shown in treating them. Fournier's dictum holds good here—to strike hard, quick and often—if good results are to be obtained.

Certain clinical signs should always suggest syphilis of the nervous system. Hemiplegia occurring in patients under forty,

who are without cardiac or renal disease, should always cause a suspicion of syphilis. The gradual development of a spastic paraplegia of the legs without sensory changes, or the sudden or slow development of eye muscle palsies, is also strongly suggestive of syphilis. In nervous syphilis there is a very marked tendency for the symptoms to regress and recur and to change their distribution. It has been said that a multiplicity of symptoms is characteristic of nervous syphilis. The reason for this is that different planes are involved, either simultaneously or at different times.

It is also to be noted that nervous syphilis produces no symptoms which may not be called forth by other causes. Examples of this are to be observed in tumors of the brain and cord as well as multiple sclerosis, all of which may simulate nervous syphilis very closely. It must also be remembered that not every organic nervous disease in a syphilitic is of specific origin. An example of this is the *pseudo-tabes alcoholica* of Bourdon, which is almost impossible to distinguish clinically from the tabes caused by syphilis.

Likewise, in nervous syphilis it is important to remember that it can parallel in clinical display any of the functional or organic diseases of the central or peripheral nervous system. It is also well to bear in mind that there are many nervous lesions which syphilis originates but which do not present the clear-cut clinical pictures such as we see in paresis and tabes. It can be taken for granted that the nervous diseases of syphilitic origin that do not exhibit the pathognomonic symptoms which are accredited to them are far more numerous than is imagined. I will go so far as to say that one may suspect a luetic origin in every *neuropathy* arising without obvious cause.

It has been observed that leukocytosis of the cerebrospinal fluid is one of the earliest signs of organic disease of the nervous system. It is also found in multiple sclerosis and other diseases not due to syphilis. On the other hand it is important to note that leukocytosis is not found in functional neuroses. This leukocytosis is a reaction due to the presence of degeneration products in the cerebrospinal fluid. The higher the leukocytosis the greater the degree of inflammation and the more recent. It indicates an acute process and as such is of favorable prognostic import as compared to a low leukocyte count which indicates that the acute process is passed and that the degenerative process is complete. This leukocytosis occurs early in the disease and signifies a meningeal reaction although no symptoms may be present. It frequently corresponds to the period of the cutaneous eruption. Dreyfus found changes in the spinal fluid in 80 per cent of all cases of secondary syphilis examined by him. These changes consisted of leuko-

cytosis, increase of the globulin content and often increased pressure as measured by the manometer.

Extensive investigations made by Wile and Stokes show that all cases of syphilis which reach the secondary stage (the exceptions being those which have been aborted by treatment, and of these some, while in the preëruptive stage) receive from the primary focus a hematogenous infection which must of necessity reach the nervous system as well as the other viscera. In view of this fact how can we explain the occurrence of manifestations in some instances and perfect freedom of the nervous system in others? Two theories have been advanced as explaining this. One is that a special strain of treponemata which has a predilection for the nervous system causes the symptoms of nervous syphilis to develop. The other is that nervous syphilis is due to the susceptibility of the nervous system in certain individuals. That is to say, that where these manifestations are present the treponemata have fallen on fertile soil. From this standpoint it is proper to assume that nervous syphilis, early or late, develops in those in whom the treponemata have early made an impress on the nervous elements. It is with this view that I am in accord. That there is a special strain of the organisms which has a predilection for the nervous system, as I have stated elsewhere, I utterly deny.

The great frequency with which Wile and Stokes found definite changes in the spinal fluid without any manifest objective symptoms of involvement of the nervous system indicates, it would seem, that for the most part the involvement of the nervous system, which occurs in early syphilis is of an ephemeral character. It would also seem, therefore, that the fate of every syphilitic, in so far as the integrity of his nervous system is concerned, is determined very largely in the first months of the infection, since it is then that the nervous system undoubtedly receives its quota of treponemata.

Mathauschek and Pilcz have presented statistics showing that paresis and tabes occurred in cases which in their early stages were treated inadequately or not at all. This confirms the statement made by Fournier many years ago.

With all the emphasis at my command, I would say that any case which shows, either objectively or from the evidence obtained from the spinal fluid, that the nervous system is involved even at the onset of the disease should be considered a potential tabetic or paretic, and should receive in conjunction with arsphenamine and mercury in the usual way—intraspinous injections of arsphenamine as well—until the spinal fluid is normal.

As I have already said, it is undoubtedly true that there exists in the nervous system a tendency to latency and to the slow and

insidious evolution of these nervous manifestations. Observations made from such a large number of cases, that the fact is undeniable, show that the fate of every syphilitic in regard to cerebrospinal lues is determined in the first months of the infection. This has been known clinically as long as these manifestations have been carefully studied. The isolated palsies, hemiplegia, monoplegia and other nervous symptoms that have been noted early in the disease were formerly assumed to be due to precocity rather than as a part of the secondary syndrome. It was not until the spinal fluid had been exhaustively studied in the early phase of the infection that the true reason of this early involvement was thoroughly understood. Ravaut, Widal and Sicard, even before the Wassermann reaction was discovered, described marked chemical and cellular changes in the cerebrospinal fluid of syphilitics, both in the early and late stages. Ravaut found a very high percentage of involvement of the spinal fluid early in the secondary stage. So high and constant was this involvement that he asserts that the nervous system is affected in from 60 to 70 per cent of all cases in the secondary stage. Altman and Dreyfus, in a series of 36 cases of secondary syphilis in which lumbar puncture and examination of the spinal fluid was done, found only 22 per cent in which it could be said that the fluid was normal—that is, 78 per cent showed involvement of the nervous system as evidenced by the spinal fluid.

In common with other protozoal diseases, notably "sleeping sickness," the Treponema pallidum undoubtedly singles out the nervous system for its fiercest attack. This was recognized as long ago as 1902 by Brissaud, who observed the predilection of the disease for ectodermic structures. When we realize that the undoubted dissemination of the treponema is hematogenous it is not difficult to understand how and why it attacks the nervous system.

That this occurs very early in the course of the infection is exemplified by a case cited by Schamberg of a young man with a roseola, in whom there was also difficulty of speech and deglutition, ataxia and other symptoms resembling disseminated multiple sclerosis, which promptly disappeared under the influence of arsphenamine and mercury.

The statistics gathered by Naunyn, in 1888, are of the utmost importance in regard to the early development of nervous syphilis and its prognosis. His material consisted of 326 cases, including 70 necropsies, all of which was carefully selected and tabulated. His object was to determine the prognosis of luetic neuroses. In considering the prognosis of a give case he attached importance to the following: (1) The age of the patient—the younger the patient the better the prognosis; (2) the age of the infection—the

less time it had existed the better the prognosis; (3) the time which had elapsed between the last other manifestation of syphilis and the appearance of the syphilitic nervous disease; (4) the duration of the nervous symptoms before energetic antisyphilitic treatment had been given—the longer the symptoms had existed without treatment the less favorable was the prognosis; (5) the form in which the disease was manifest; (6) whether the patient had received any treatment or not previous to the appearance of the nervous lesion. He selected only those cases concerning which definite data were obtainable and from the literature on the subject he was able to obtain only 290 cases which met his requirements in this respect. Out of 88 cases observed by himself these requirements were met only in 45. He excluded tabes, paresis and polyneuritis, as he had only prognosis in view, his experience being that in these three conditions mercurial treatment was either useless or harmful. I might add that the facts, as arranged by Naunyn, to a very great extent still hold good, although they were intended for a past generation who knew not arsphenamine, the Wassermann reaction or other tests of today.

These carefully compiled statistics of Naunyn demonstrated beyond all question of a doubt that syphilitic disease of the nervous system appears most frequently during the first year after the initial lesion, that this frequency diminishes from year to year, and also that during the first year this frequency is greater during the first six months than during the second six months.

The data later gathered by Erb are in accord with those of Naunyn. Of 22 cases reported by him, in which the date of the infection was known, 59 per cent appeared during the first three years and 82 per cent during the first six years.

The lesson to be learned from the study of this problem of syphilis is plain. It is that nervous syphilis is more often present either active or latent, especially the latter, than is usually supposed; also that its presence should be searched for if we are to do our full duty by our patient in *every* case of syphilis, whether attended with symptoms referred to the nervous system or not. If found it should be attacked promptly and with all the means at our disposal, including intraspinous therapy in every instance. Also that the prognosis in these early cases, if properly diagnosed and treated at the beginning, is good; this is all the more reason why these cases should be treated intelligently and energetically. In this particular instance in antiluetic therapeutics, these two terms are synonomous.

CHAPTER XI.

LATE SECONDARY SYPHILIS.

The arbitrary division of the syphilitic life cycle into three stages as was first done by Ricord is, in the main, pathologically and clinically correct. At the same time, as every syphilologist knows, secondary symptoms may be manifest before the completion of the first stage, that is, before the chancre has healed; or tertiary symptoms may present themselves during the secondary period; or secondary symptoms may appear during the period when we would otherwise expect only symptoms of tertiarism. It is with this last type that we will here concern ourselves.

The normal limit of the secondary stage of syphilis is approximately three years. After that time lesions assume what we term the tertiary type. That is, from comparatively benign processes attacking the skin and mucous membranes, they change and become more destructive with a marked tendency to attack the deeper structures of the body, the bones, viscera and nervous system. But, as I have already stated, the line of demarcation between the two stages is not always distinct and sharply drawn. In about 6 per cent of all cases of syphilis secondary symptoms continue to appear in what from the point of time may be correctly designated as the tertiary stage It is undoubtedly true as statistics have shown that the later the period after the third year the fewer these lesions are. In a series of cases analyzed by Fournier, in the fourth year there were 266 cases; in the fifth, 194; in the sixth, 133; in the ninth, 67; in the tenth, 36; in the thirteenth, fourteenth and fifteenth, 8. If these figures be plotted in a curve it will show that the descent is rapid from the fourth to the eleventh year, after which the descent is so gentle as hardly to be considered. In other words, for the first seven or eight years the lesions, while frequent, show a steady diminution, but after that time the date of their appearance is of no significance, for they may be encountered with about the same frequency in any year thereafter. A fact also to be remembered is that the contagiousness of these lesions is not parallel with their incidence. They are much less so than secondary lesions occurring during the time in the natural evolution of the disease that they usually appear. The period of time during which these secondary relapses may occur sometimes

extends over very many years. Fournier recorded a case of late secondaries occurring thirty-one years after infection, and I have seen them occur fifteen years later. Since there is no reason to doubt that these outbreaks may occur at no matter how remote a time from infection, there must be a cause for this erratic manifestation of the disease. It is by no means easy to diagnose these late secondaries—the later they appear the more difficult this becomes. They possess certain characteristics, however, which are worthy of note as aids in making a diagnosis. Of these, one is their tendency to reappear continually in the same clinical form, such as mucous papules in the mouth, and palmar syphilides. Another striking feature about them is that they yield to treatment with startling rapidity; sometimes they vanish in two or three days.

It is quite apparent, therefore, that these late secondaries indicate that the patient is far from being cured; they also show that the virulence of the disease is low. Fournier's hypothesis is that they represent a syphilis that has been modified by treatment. With him I am in accord. These patients are usually in far better physical condition and offer a better prognosis as to ultimate cure than those who are victims of true tertiary lesions or who have coexisting tertiary lesions along with the late secondaries. These we know are, in the vast majority of instances, the result of half-treated or untreated syphilis. However, I do not wish to infer that every case of late secondaries has been well treated; but what I mean is that in theory we may assume that whatever the degree of treatment has been it has been beneficial. This is borne out by facts laboriously collated by Fournier. In a series of 581 cases of late secondary manifestations with data of treatment, there was abundant evidence that the majority of them had been well treated with mercury at the start (this was before the advent of arsphenamine) or during the first three years of the disease. Some 229 cases had received treatment for more than two years, and 144 had received treatment for more than one year. Only 1 patient had received no treatment whatsoever. The analysis of these cases showed that the greater the duration of the treatment the more numerous were the cases of late secondary syphilis—a paradox which may explain the ancient belief that mercury aggravated the disease and was even the essential cause of secondary syphilis. But it must also be stated that the same phenomenon occurs after treatment with arsphenamine, so it is evident that the cause must be sought for elsewhere.

From the nature of these lesions it is the skin and mucous surfaces that are attacked. Practically every form of skin syphilide is represented. But although they occur as typical secondaries, yet there is a certain difference between them and the originals.

Their benign quality has been already noted, they are also peculiar in their tendency to always assume circinate patterns. They are frequently abortive. They are also more circumscribed and not so diffuse in comparison with the early outbreak. In other words, they represent a more or less involutional type. The disease has been reduced as it were to lower terms.

In passing I may add that it is quite possible that the phenomenon of allergy could be invoked to explain the presence of these lesions, the skin having been sensitized by the toxins reacting from time to time against the minimal production of the latter. But since allergy is purely a phenomenon of the skin, this does not explain the mucous lesions.

Palmar and Plantar Syphilides.—The late secondary lesions most frequently encountered are palmar and plantar syphilides. Unlike other late secondary lesions they are somewhat refractory to treatment. These late secondary syphilides must not, however, be mistaken for the tertiary lesions occurring on the palms and soles which are in strict accord with the period of their development. There are many ways of discrimination. Thus, the characteristics of the early lesions are upheld in the late secondary manifestations. These syphilides are irregular in outline and of a deep red color. Sometimes small masses of epithelium are imbedded in them. In some instances there is desquamation; more frequently there is not. The real tertiary palmar or plantar syphilide has characteristics of its own. The skin is much more thickened and hard; it is parchment-like or even leathery. Desquamation in layers is seen. Fissures and rhagades occur in the natural folds of the fingers and toes and at the plantar or palmar junction; tubercular syphilides are sometimes seen. In the true tertiary type either the soles or palms are attacked alone, whereas in the late secondaries both parts are usually affected.

These late secondaries attacking the palms and soles occur in three well-marked forms. The first and most primitive is the discrete papule, a number of which are scattered over the surface of the part affected. The name lenticular has been given to these small papules, which are rounded, dry, with a scaly covering which at times desquamates, leaving a so-called collarette bounding the denuded surface.

In the second form the isolated papules, such as occur in the first, become confluent and form several patches of irregular outline. As with the lenticular papule the surface may be covered with epithelial scales, or it may be bare and surrounded with the collarette. In some cases the entire palm or sole may be covered with the syphilide.

The third or circinate form presents two varieties, one of which

is merely a circinate grouping of papules while the other is a continuous circinate formation which curves along the palm or sole and represents a coalescence of a continuous line of papules. These circinate formations sometimes delineate separate curves separated by healthy areas. In rare instances they form a complete ring. The eruption not infrequently extends to the fingers.

Roseola.—A rare occurrence is a palmar roseola—a mere hyperemic blush confined to a few scattered papules. This can hardy be termed a syphilide, but rather an abortive attempt. It sometimes represents the last of a series of more pronounced attacks.

A roseola is usually one of the earliest manifestations of secondary syphilis. But the roseola is included in the manifestations of the late secondaries. In this instance, however, it is considerably modified from the rash occurring in the earlier stage of the disease. It is circumscribed and limited to certain areas and inclines to present a circinate grouping. There are two forms. In one the roseola is very faint—as if it had been and was fading. The lesions are large and discrete, limited in number so that they can be easily counted. They are to be found on the abdomen, thorax, back or segment of a limb. They are about the size of a silver dollar. They are sometimes so pale that it is difficult to makle them out with the naked eye. Where these lesions are suspected the surface of the body should be examined through a piece of blue glass. The other form is distinctly circinate in appearance with a tendency to occur in groups. Unless treated these lesions are extremely persistent. My experience has been that these eruptions are more frequent in females.

All of these roseolas show a decided tendency to relapse, especially if treated with mercury alone. If properly treated, however, the recurrences after each succeeding relapse will be fainter and less distinctive than the preceding, and finally they will cease altogether.

Erythema.—A late secondary of interest because of its rarity is erythema. It is seen in all localities except the face. It usually appears as a mere redness. It is always circumscribed and discrete. The spots are by no means numerous and a pattern can be usually discerned in the grouping of them. Like all late secondary eruptions they show a circinate tendency. These erythematous spots are usually persistent and show only a slight tendency to relapse. A peculiar characteristic of this type of late secondary is its occurrence side by side with tertiary lesions of the most pronounced kind. The condition also persists after these have been healed. Another characteristic of this form of erythema is that it is frequently encountered with tertiaries of extra severity. The erythema in itself is of slight consequence but the regularity with which it

occurs in severe and refractory tertiary lesions enables us, upon its discovery, to so prognosticate. This being the case the diagnosis of this form of late secondary is of extreme importance. Its resemblance to ringworm and other circinate affections is most striking. The number of dermatoses which exceptionally assume a circinate form is considerable and it must be differentiated from them. Among these are polymorphous erythema, pityriasis rosea, seborrheic eczema, psoriasis and lepra. Braumann's studies show that most of these cases have been previously well treated; but it has also been asserted that it is found with equal frequency in cases which have received little or no previous treatment.

I must confess that I do not know whether to include this late erythema with the late roseolas or to separate it thereform. It is a difficult question to decide although there are numerous points of dissimilarity. The points of resemblance are also obvious.

Late secondaries in the form of discrete papulo-crustaceous lesions may appear in the scalp. They are for the most part scattered and small. They are obstinate to treatment and prone to relapse.

Lesions of the Nails.—Lesions of the finger and toe-nails are also sometimes seen as a late secondary manifestation. All of the nails may be affected or only one or several. They may present as a simple onychia with a dry induration or the nail may be separated and shed. The nail may be only thickened. It may also take the form of a perionychia in which the nail proper is spared.

Mucous Membranes.—Late secondary lesions of the mucous membranes are more than common. Their occurrence in the tertiary stage of the disease is most momentous, especially if the patient is married or contemplates entering the marital state. It is well known that the so-called mucous patch is the most fertile source of infection because it is perhaps in the highest degree the most contagious of syphilitic lesions. While we know that contagion is lessened or annihilated in the tertiary stage, the presence of these lesions gives rise to a paradox that is both difficult to understand and to overcome.

Mouth.—Undoubtedly because of the constant irritation from tobacco, alcohol and bad teeth, the buccal mucous membrane is a favorite site for these lesions. The tongue is the part most frequently affected—to be exact, in 85 per cent of all cases. The remainder occur on the lips, fauces and palate. The usual form the lesions take is that of a small—sometimes almost herpetiform—round erosion, either red or gray in color. They do not differ from those typically seen in the secondary stage of the disease. As a rule they are not accompanied with any other manifestations of tertiary syphilis, which may sometimes make diagnosis difficult in view of the fact that the number of lesions of the buccal surface

which are not syphilitic is considerable—the so-called "cankers" from mechanical causes, herpes, and a host of general rashes accompanied with buccal localization. In these obscure cases we must often have recourse to either the treatment test or the serological. They must be treated with respect, however, no matter how abortive and insignificant they may appear, for they are contagious and therefore a social menace.

Tongue.—Another form of late secondary, which not infrequently attacks the tongue, is a form of glossitis. This is a true late secondary which must be sharply differentiated from the numerous tertiary lesions which attack the organ. Like all other secondary lesions, it is very superficial. It may be likened to a desquamation rather than to an erosion. The first impression is the morbid discoloration. This is red or brown or even bright carmine. It is like a bald spot on the tongue if we regard the papillæ as so many hairs. Or it may be likened to a scraped or shaved surface. This bareness of appearance is due to the destruction of the horny prolongations of the papillæ—an alopecia of the dorsum of the tongue as it were. The contours of these denuded patches are always well defined. Otherwise they have no distinctive features. The process is a dry one, and the lesions have been called dry mucous patches. Some of these patches are lenticular in size, while others may be as large as a twenty-five-cent piece. As a rule, the lesions are found on the anterior part of the tongue. Sometimes there is a single large lesion which may occupy the whole anterior half or third of the tongue, or it may form a ribbon-like band around the edge of the organ. When the lesions are lenticular they sometimes assume the circinate arrangement which seems to be a characteristic of late secondary lesions. These lesions do not tend to appear and disappear. They are likely to become permanent unless energetically treated. It is my opinion that they not infrequently are the harbingers of a sclerosing glossitis.

Lesions on the Genitals.—Late secondaries occurring on the genitals are of interest because, while not especially frequent, when they do occur they are frequent sources of infection at a time when infection is supposed to be reduced to a minimum. Late secondary lesions occurring on the genitals are much more frequent in men than in women. This undoubtedly accounts for many cases of marital infection occurring long after the husband was supposed to have been cured. It is also of interest as showing the comparatively slight risk in cohabiting with women with old syphilis.

In the male these lesions are seen on the penis or scrotum or both—on the penis more frequently than on the scrotum. They may be represented by a simple erythema or a papular or papulosquamous eruption. The sulcus and the cutaneous covering of the

organ are the locations usually involved. For some reason the glans is usually exempt. The papules are dry and bear no resemblance to the mucous patch. They vary much in size—some being lenticular, while others cover an area as large as a lima bean. There is very little desquamation and no crust formation. When lenticular in size the characteristic circinate formation is sometimes seen.

In addition to the dry papules just described there are also erosive lesions. These may be simple erosions or erosive papules. They are often difficult to diagnose from slight traumatisms and from herpes progenitalis. To make the diagnosis still more difficult, herpes progenitalis is not infrequently associated with these late secondaries and assumes the geographical or circinate outline characteristic of the syphilitic lesion, the only point of distinction being that in herpes the circles are on a small scale.

Late secondary syphilides on the scrotum resemble in every way the early secondary lesions, such as occur on the scrotum within the first two years of the disease. They may appear as circinate, lenticular, dry, slightly desquamating papules or as moist, confluent patches, not infrequently complicated with eczema. The eczematous condition sometimes overshadows the syphilitic, but when it subsides, as it does under proper treatment, the characteristic mucous patches again come into prominence.

Late secondaries on the genitals of women are, as I have already stated, comparatively rare. When seen they assume the general appearance of the mucous patch such as is so frequently encountered in the early months or years of the disease.

CHAPTER XII.

THE TERTIARY STAGE OF SYPHILIS.

Tertiary syphilis is an evolution of secondary syphilis. It is essentially a chronic condition—a dyscrasia characterized by symptoms of various kinds, many of which, superficially at least, seem to have no relation whatsoever to the disease. For this reason it is hardly possible to write a clear clinical history of tertiary syphilis. At this stage the disease rarely attacks two individuals alike and the symptoms when they occur are without order or arrangement, and are most irregular in their appearance as to time and place. It is from generalizations, therefore, deduced from vast numbers of cases that we are enabled to reach conclusions of the extent and course of the morbid processes that constitute its phenomena. Secondary syphilis partakes of the nature of a more or less acute disease, in which the symptoms appear with a certain degree of regular sequence. Also, in secondary syphilis the tendency is for the lesions to undergo resolution; whereas in tertiary syphilis there is no regularity in the appearance of the symptoms which are always more or less chronic; neither do they show a tendency to heal, but rather one of increasing destructiveness.

It by no means follows that every case of syphilis evolutes to this stage. The fact is that the majority—the vast majority—do not. It is difficult to estimate the percentage of syphilitics who develop tertiary symptoms, but the consensus of opinion is that it approximates from 15 to 20 per cent. As a general rule, tertiary syphilis develops when the treatment has been inadequate in the secondary stage, but this does not always follow. About 5 per cent of all cases of tertiary syphilis have received adequate treatment. Tertiary symptoms usually appear within three to five years after the appearance of the chancre. After the secondary outbreak has subsided there is often a period of quiescence between the two stages, during which time the patient is entirely free from symptoms except that his blood reacts positively to the Wassermann test. The reason for this temporary subsidence in the activity of the disease is unknown. It was pointed out by Virchow nearly seventy years ago and commented upon by him; but even he, the greatest of pathologists, could offer no satisfactory explanation of its cause.

Early Tertiary Symptoms.—In a certain small proportion of cases tertiary symptoms appear precociously—within a few months after the chancre. This type of syphilis runs a very rapid and malignant course, and may terminate in death. It is needless to state, however, that this raising of the disease to the *n*th degree of virulence as it were, is rare—so rare indeed, that it need only be mentioned as a most remote contingency. Formerly such cases were much more frequent, as anyone who has read the books of a hundred or even fifty years ago can testify. It is not infrequent for tertiary symptoms to manifest themselves within the first year of the infection and when this is so the lesions are usually severe, but far from being lethal. In these cases of early tertiary manifestations—usually cutaneous—there is almost invariably some underlying dyscrasia which has profoundly weakened the systemic resistance so that it falls an easy prey to the ravages of the disease. Destructive ulcers form—the primary lesion may be of that character (the so-called phagedenic chancre)—which are slow to heal. Nervous symptoms of a severe type may early appear. In these cases there is, as a rule, absence of roseola, mucous patches and alopecia. The secondary stage seems to be skipped as it were; the disease passing directly from the primary to the tertiary stage. Also, strange to say, it often happens that these cases, which are attended with such a severe initiatory outbreak, usually end in recovery—not only clinically but serologically as well. Here again, we have one of the enigmas of syphilis.

After the tenth year tertiary symptoms occur with ever-increasing rarity as the years elapse, although tertiary outbreaks have been known to have occurred more than fifty years after the chancre. In the tertiary stage syphilis manifests itself in the following order: the nervous system, the bones, the skin and mucous membranes and the viscera. Many of its symptoms are extremely occult and are masked by other diseases, of which, however, it is the essential cause. These phases of the disease are discussed at length in other chapters of this book.

Tertiary syphilis always implies destructive or atrophic changes. This is due to the nature of the pathologic processes at this stage, the gumma and the proliferative inflammation. The gumma destroys by ulceration, and the proliferative inflammation later changes to fibrous tissue, thereby producing sclerosis of important structures, such as the liver, the cardiovascular system, as well as productive osteitis, interstitial orchitis, bronchiectasis, meningo-encephalitis and degeneration of the cord and its membranes, all of which are characterized by symptoms peculiar to the part affected. Tertiary syphilis, however, in its attack is often purely local. This is exemplified when the disease is focussed as it were upon some locality

or part, such as a gumma of the soft palate, the testicle or an isolated gummatous ulcer somewhere on the cutaneous surface, the patient being otherwise in excellent health. Quite frequently these local lesions have an appreciable local cause in some point of irritation.

Tubercular Syphilide and Gumma.—While tertiary skin lesions are comparatively frequent, cutaneous syphilides usually occur in but two varieties. These are the tubercular syphilide and the gumma. The distinction between these two is mainly one of size; but further, the tubercular syphilide is intracutaneous and the gumma subcutaneous. Syphilitic tubercles are small, red, copper-colored

FIG. 22.—Gummatous ulcer of the scalp. (Courtesy of Dr. M. B. Parounagian.

nodules of the skin which may or may not break down and ulcerate. In arrangement they are either serpiginous or circinate—most frequently the latter. In fact the circinate appearance, which most of them have, is a most important element in their diagnosis. They appear as more or less complete circles or segments of circles, irregularly and asymmetrically situated on the surface of the body. They have no special predilection for any part of the body. When appearing on the face they not infrequently assume a corymbiform shape and are then often mistaken for lupus erythematosus. The gumma is considerably larger than the tubercle and begins beneath the skin. It may vary in size from a lima bean to a hen's egg,

FIG. 23.—Gumma of the forehead. (Courtesy of Dr. M. B. Parounagian)

FIG. 24.—Gumma of the upper lip. (Courtesy of Dr. M. B. Parounagian.)

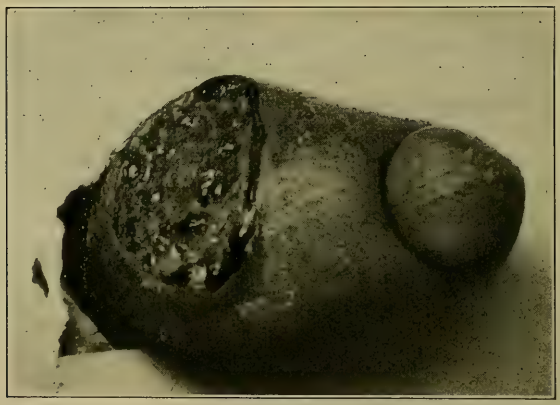


FIG. 25.—Gumma of the penis. (Courtesy of Dr. M. B. Parounagian.)

and is usually sharply circumscribed. It is really a granulative neoplasm and in the early stage of its development is often mistaken for a cold abscess. Later the skin immediately over it becomes first livid and then a deep red and finally breaks down, leaving a clear-cut, deeply excavated ulcer, the floor of which is covered with necrotic débris. Several gummata may form in continuity and

FIG. 26.—Serpiginous ulcerative gumma. (Courtesy of Dr. M. B. Parounagian.)

coalesce, making an extensive ulcerating surface. Not infrequently a gumma may form in the female breast, and as such be diagnosed as a malignant growth. The same is true of the lip, the tongue and other parts of the body. Gummata differ from malignant neoplasms in that they are painless, are not hard or infiltrated, and the neighboring glands are not enlarged. Gummata

FIG. 27.—Serpiginous gumma. Note the healed areas. (Courtesy of Dr. M. B. Parounagian.)

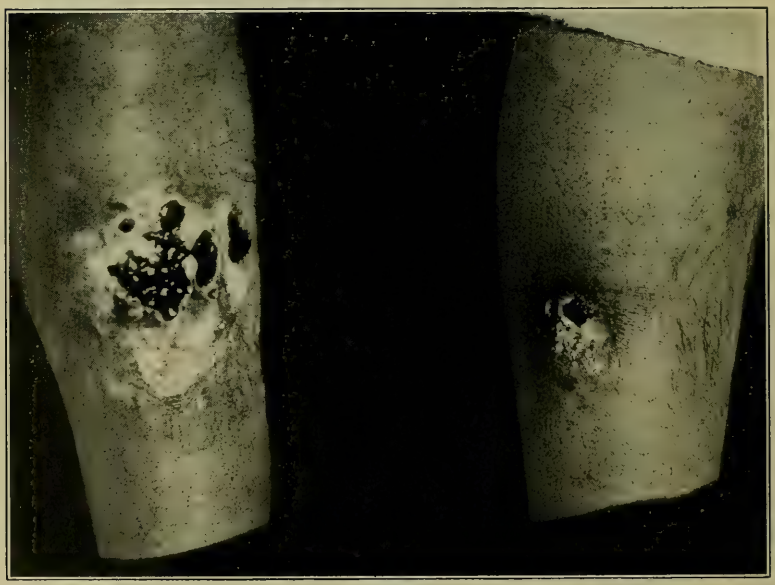


FIG. 28.—Gumma of the legs. (Courtesy of Dr. M. B. Parounagian.)

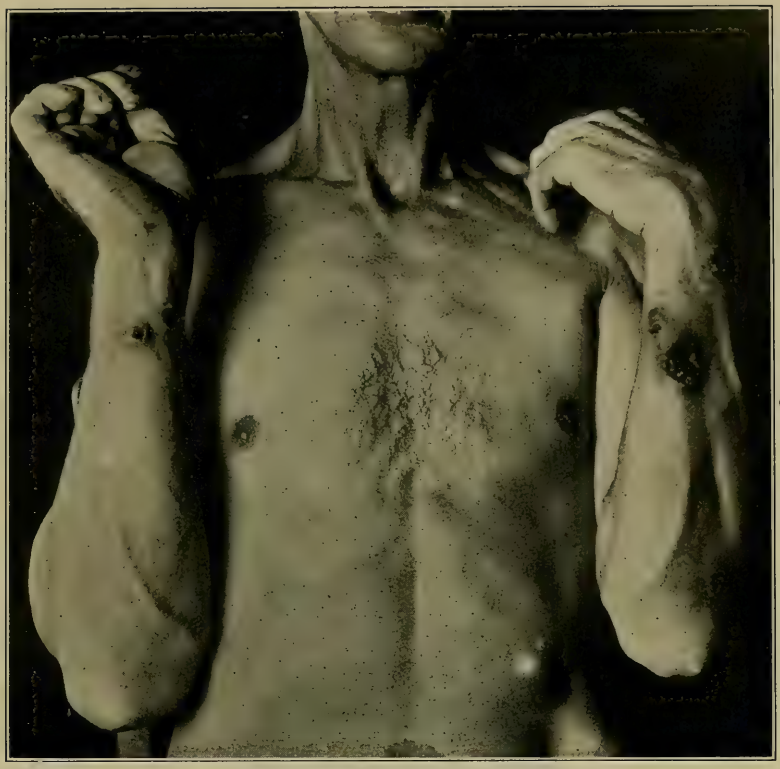


FIG. 29.—Ulcerating gumma of the forearm. (Courtesy of Dr. M. B. Parounagian.)

FIG. 30.—Gummatous infiltration simulating lupus. (Courtesy of Dr. M. B. Parounagian.)

occurring on the face or lower extremities not infrequently have erysipelas superimposed upon them. When occurring on the leg a gummatous ulcer may be mistaken for a varicose ulcer, especially if varices are present. It is to be remembered in this connection in differentiating between them that if the ulcer occurs above the lower third of the leg it is probably syphilitic because varicose ulcers are never found situated so high.

FIG. 31.—Serpiginous gumma. (Courtesy of Dr. M. B. Parounagian.)

Gumma of the Tongue.—In tertiary syphilis a gumma may form in the tongue, or that organ may undergo sclerosis. Gumma of the tongue is felt at the onset as a small tumor in the musculature which later breaks down, leaving the ulcer. It may be in the midline or on either side. It is painless and there is no glandular enlargement and by these clinical signs is to be diagnosed from epithelioma. The sclerotic induration is preceded by an infiltration whereby the tongue first increases in size. It feels thick and

is indented on the sides by the teeth and speech and deglutition are more or less interfered with. When the inflammation sub-

FIG. 32.—Leukoplakia. (Courtesy of Dr. M. B. Parounagian.)

FIG. 33.—Leukoplakia. (Courtesy of Dr. M. B. Parounagian.)

sides the organ atrophies and hardens and when this occurs its appearance is very typical. Indurative atrophy of the tongue is frequently caused by tertiary syphilis and is a clinical sign of much importance as pointed out long ago by Virchow and more recently by Symmers.

Gumma of the Soft Palate.—A gumma may attack the soft palate. The onset is insidious, and great damage may be done before the patient is aware of it, because of the entire lack of pain. It is surprising how quickly a gumma in this locality will cause a perforation. The velum and uvula may be destroyed. Communication between the nose and mouth may take place, converting the two into a single cavity sometimes, interfering with deglution and giving the voice a peculiar note. Gummatous ulceration of the nasopharynx may suggest tuberculosis, but the rapidity of the destructive process and the absence of pain are clinical aids of great advantage in the differential diagnosis without the assistance of the Wassermann test.

Tertiary Syphilis of the Larynx.—Tertiary syphilis is sometimes manifest in the larynx. The lesions may be ulcerative and destructive, or there may be an infiltrative thickening of the mucous membrane. The principal symptoms to be noted are dyspnea and a throaty hoarseness of the voice.

Stricture of the esophagus is sometimes the result of cicatricial bands, following a gummatous infiltration, and the symptoms caused thereby do not differ from those arising from some other cause—trauma, the pressure of a growth or from carcinoma. In carcinoma there is usually a more profound and characteristic cachexia than is present in tertiary syphilis.

Tertiary Syphilis of the Respiratory Tract.—The organs of respiration—the trachea, bronchi and lungs—are sometimes attacked by tertiary syphilis. While not often encountered (and still less frequently diagnosed), they occur with more frequency than is usually supposed. When the trachea is involved it is usually manifest by stricture which gives rise to hoarseness and aphonia, dyspnea and swelling of the jugulars with expiration. A downward movement of the larynx can also be noted with inspiration. With the stethoscope inspiratory stridor and weak breathing can be detected. In most text-books syphilis of the lungs receives but scant attention. It is generally supposed to be a form of syphilis that is extremely rare. I do not hold this view. So much am I impressed with its comparative frequency and consequent importance as one of the manifestations of tertiary syphilis that I have discussed it at length in a separate chapter. Suffice it to say here, that syphilis of the lungs is frequently mistaken for tuberculosis with which it is sometimes associated. Where syphilis of the lungs is sus-

pected the case should be thoroughly studied and the diagnosis absolutely confirmed because of the harm that can be done to a patient with tuberculous disease by the administration of mercury and potassium iodide. The physical signs afford little if any help, but it is to be noted that the lesions of syphilis tend to be basal rather than apical, the reverse being the case in tuberculosis. The sputum should be frequently examined, especially if large amounts of broken-down tissue are coughed up. The roentgen ray should not be omitted as an aid to diagnosis. Bronchiectasis is no doubt at times caused by syphilis and the same holds true, in my opinion, of so-called abscess of the lung. Syphilitic pleuritis not infrequently accompanies syphilis of the lungs.

Tertiary Cardiac Syphilis.—Tertiary cardiac syphilis is much more frequent than is usually supposed. The disease may attack the pericardium, the myocardium and the endocardium. The symptoms are practically the same as when arising from other causes. Syphilis of the heart should be suspected in the presence of cardiac failure occurring in young or middle-aged persons, in whom no history of rheumatism can be obtained. Symptoms of angina in young persons are always strongly indicative of cardiac syphilis.

Syphilis of the Arteries.—The arteries are particularly prone to be pathologically affected by long-continued syphilitic disease. Syphilis, aside from old age and alcoholism, is the most important factor in causing arteriosclerosis. Atheromatous changes, circumscribed areas of degeneration in the vessel walls may cause aneurysms both of the large and small arteries. For, it may be said without fear of denial that every aneurysm, unless caused by trauma, is due to syphilis. This applies not only to the aorta but to such arteries as the lenticulo-striate which, when aneurysmal, gives rise to scotoma. Arterial disease of the vessels supplying the brain and cord enters very largely into the syndromes generally grouped as nervous syphilis.

Syphilis of the Liver.—Of the organs situated in the abdominal cavity, the liver is more frequently attacked by tertiary syphilis than any other viscus. Syphilis may cause amyloid degeneration, perihepatitis or hepatitis—either diffuse or gummatous. The organ may be enlarged and nodular from the presence of gummatous masses, or it may be diminished in size from cicatricial contraction. There may be jaundice which is usually slight, or there may be ascites. In fact, all of the symptoms of either a hypertrophic or an atrophic cirrhosis may be observed. Albuminuria is frequently present. Also, as in all hepatic diseases, the patient is inclined to be mentally depressed. The symptoms of syphilitic disease of the liver are of slow approach and a long time usually elapses before the patient complains. Syphilitic cirrhosis of the liver is

to be diagnosed from carcinoma by its slower development, the absence of cachexia and the almost invariable presence of albuminuria which may not be present in malignancy. The prognosis of syphilitic cirrhosis in the advanced stage is not good, although in the active gummatous stage energetic treatment may cause the neoplasms to disappear entirely.

Syphilis of the Spleen.—In secondary syphilis the spleen is enlarged temporarily, but the enlargement soon subsides. In the tertiary stage the organ may be the seat of either a gumma or of a gummatous infiltration which later undergoes sclerosis. There are no special symptoms connected with it and the lesion is usually discovered at necropsy. Gummatous infiltration of the spleen usually involves the peritoneum as well, causing adhesions to form.

Syphilis of the Stomach.—There are no pathognomonic symptoms of tertiary syphilis of the stomach; although Hemmeter holds that "in tertiary syphilis the remarkable malnutrition is due to a chronic gastritis." Tertiary syphilis undoubtedly causes gastric ulcer, and it can also be said that many so-called malignant tumors are in many instances nothing more than gummatous masses.

Syphilis of the Intestines.—Tertiary syphilis of the intestines is rare, although it is possible that it can occur. Certain cases of duodenal ulcer are, I believe, of syphilitic origin. In the tertiary stage the disease invades the rectum either as a gumma or as a diffuse infiltrative inflammation. A gumma of the rectum does not differ in its characteristics from a gumma occurring elsewhere. It is found most frequently just above the internal sphincter muscle. Owing to the ease with which infection can take place at this site gummata of the rectum sometimes become phagedenic. They may then resemble chancroid or carcinoma. When these lesions heal a stricture is the inevitable result; but where there is a perirectal infiltration stricture is less likely to follow. Tertiary syphilis of the rectum is observed more frequently in females than in males and in not a few instances is accompanied with evidences of amyloid degeneration of the liver, spleen or kidneys.

Syphilis of the Genito-urinary Tract.—Gummata of the kidneys occurs but, as a rule, are only discovered at necropsy. Sclerosis of the kidney—the "small red kidney"—is undoubtedly caused by syphilis, although in many instances absolute proof is wanting. The adrenals are more frequently attacked and the phenomena produced in such instances I have discussed under the heading of "Syphilis and Endocrine Diseases." The bladder is rarely the seat of a gumma, although cases have been reported. The same is true of the prostate. Thompson has collected a series of cases in the literature extending back for a period of many years. Some of these undoubtedly represent such a phase of the disease, while others are, in my opinion, open to doubt.

The epididymis and testis are sometimes attacked by syphilis in the tertiary stage. When the epididymis is involved there is a slow and painless enlargement of the globus major. Syphilitic epididymitis is to be distinguished from that caused by gonorrhea and tuberculosis. In the former there is usually a history of a recent discharge and the process is much more acute; in the latter there are usually evidences of tuberculous infection elsewhere, most frequently in the lungs, also there is almost always sinus formation and the globus minor is usually first attacked. Syphilitic orchitis is usually painless and insidious in its onset. The testicle slowly enlarges and the patient only complains of a feeling of weight and dragging on the cord. The condition known as fungus of the testicle consists of an excessive exuberance of granulation tissue where the gumma has broken through the scrotal integument. It has the appearance of a fleshy tumor, narrow at its base, exuding pus and covered with necrotic detritus. In some instances the gumma is absorbed, leaving the gland sclerotic and atrophied, causing impotence or reduced sexual desire. Tertiary syphilitic disease of the testicle is to be distinguished from tuberculosis, sarcoma, epithelioma and hydrocele with thickened walls. Hydrocele, however, is not an infrequent manifestation of tertiary syphilis of the testicle. On the penis gummata sometimes occur, usually on the site of the original sore—chancre redux. These so-called relapsing chancres I have discussed in the chapter on the Chancre.

Syphilitic Myositis.—Myositis, either diffuse or gummatous, is sometimes encountered as a manifestation of tertiary syphilis. No muscle of the body is exempt, but the muscles most frequently affected are those of the arms and legs. There is more or less impairment of function, due to pain, or contractures, or both. The condition is analogous to a slowly developing phlegmon of the part, and as such may be mistakenly diagnosed. The tendon sheaths and bursæ may also become involved but, as a rule, they are not.

Syphilitic Bone Disease.—Next to the nervous system and the skin the bones are most often attacked in tertiary syphilis. The lesions showing at this stage are usually persistent and destructive. It is said that in syphilitic bone disease the bones are extremely fragile and in consequence easily broken—*fragilitas ossium*. This holds good perhaps in tabes, due to trophic changes, but not otherwise unless the bone has been weakened by loss of substance due to an ulcerative gumma or to the shedding of sequestra caused thereby. Gummatous periostitis usually attacks the long bones, the tibia especially—"the bone that syphilis loves"—the ulna, the clavicle and the flat bones of the cranium. There is nocturnal pain, tenderness on pressure and slight redness of the skin over the bone

affected, and a doughy swelling which gradually shades off into the surrounding tissue. This proliferation may absorb or it may consolidate and form an exostosis which in time becomes as hard as ivory. Such an exostoses is most frequently observed on the tibia, giving rise to the so-called "sabre shin," which when present is practically pathognomonic of syphilis. Nodes also occur, and are most frequently observed on the frontal bones. Exostoses on the internal surface of the cranial bones by pressure may cause grave nervous symptoms. Gummatous osteomyelitis may also occur, and if the process is unchecked extensive destruction of osseous tissue may take place. This syphilitic destruction of bone is most frequently observed in the bones of the nose and on the vertex of the skull. It may also occur in the bones composing the spinal column and produce a carious condition that cannot be distinguished clinically from tuberculosis. Should the osseous gumma be circumscribed as it sometimes is, it may be difficult to distinguish it clinically from osteosarcoma.

Nervous Syphilis.—The most frequent, and by far the most formidable, form whereby tertiary syphilis is made manifest is syphilis of the nervous system. Nervous syphilis is essentially a tertiary phase of the disease, although as I have already stated more or less involvement of a comparatively benign nature is sometimes seen in the secondary stage. The lesions indented on the nervous system by tertiary syphilis are permeative and destructive to a high degree. Recovery from them, as a rule, does not follow. In most instances the most that can be done is to stay their progress.

Nervous syphilis parallels in clinical display any of the functional or organic diseases of the central or peripheral nervous system with but few exceptions—multiple sclerosis and, according to Oppenheim, multiple neuritis. Recently however, Siemerling of Jena reports finding the *Treponema pallidum* in the cord and in the spinal fluid at necropsy of several patients who had died from multiple sclerosis. Syphilis also undoubtedly originates many nervous syndromes which do not present the clear-cut clinical pictures, such as we see in the essentially syphilitic psychopathy, paresis, or in the essentially syphilitic neuropathy, tabes. It can be taken for granted that the nervous diseases of syphilitic origin that do not exhibit the pathognomonic symptoms which are accredited to them are far more numerous than is imagined. I will go so far as to say that one may suspect a syphilitic etiology in every neuropathy arising without obvious cause. I desire also to impress upon the reader's mind the fact that the characteristic or pathognomonic symptoms are not usually the early symptoms. It has been said that a multiplicity of symptoms is characteristic of

syphilis. This is true because the character of the symptoms varies, and because different planes of the nervous system are involved at different times. By this I mean that syphilis can, and does, invade simultaneously or at different intervals, different components and different levels of the nervous system. All of these factors have a bearing—a most important bearing—which cannot be disregarded.

Syphilis of the spinal cord is the most frequent form of syphilitic nervous disease. In outlining the various forms of spinal syphilis I have followed here the classification of Mott because it seems to me to be the most logical from the pathologic standpoint. It is as follows: "(1) Syphilitic disease of the vertebræ. (2) Chronic syphilitic meningitis—(*a*) chronic pachymeningitis; (*b*) chronic leptomeningitis, or both may be combined. (3) Meningo-myelitis, a leptomeningitis often localized with invasion of the cord. (4) Paraplegia of acute onset, so-called acute syphilitic myelitis; for the most part this is due to softening caused by vascular disease. (5) Chronic syphilitic spinal paralysis, Erb's paralysis, but whether this really differs from meningo-myelitis dorsalis is doubted by many. (6) Meningeal and intramedullary gummatous tumor. (7) Gummatous infiltration of the roots of the cauda equina. (8) Various analogous forms simulating other nervous diseases, *e. g.*, pesudo-tabes."

To describe the symptoms of these conditions in detail is beyond the scope of this work, but it is well to remember that while there are no characteristic symptoms of syphilis of the spinal cord there are certain symptoms, which, if they occur in young adults, especially males, should cause us to suspect it. Briefly stated these are: Severe intercostal pain, worse at night; pains in the extremities with contractures of the muscles; incontinence or retention of urine; disappearance and reappearance of the reflexes, particularly the patellar reflex or that of the Achilles tendon.

Tertiary syphilis of the spinal cord is manifest most frequently as locomotor ataxia or tabes dorsalis. This terrible disease—for it is indeed terrible—is the most important, because the most frequently encountered of all syphilitic nervous syndromes. So important do I consider it in all its varying phases that I have devoted a special chapter to its consideration and will therefore forego discussing it here. Suffice it to say that the practitioner of general medicine should be thoroughly acquainted with tabes if with no other of the nervous lesions of syphilis. It is important not only because of its frequency but because of its slow and insidious, and many times atypical, advance, which, in the vast majority of instances, could be checked if diagnosed in time. For, it is to the general practitioner that these patients first present them-

selves, usually for some symptom or combination of symptoms that do not all suggest the onset of syphilitic nervous disease.

The peripheral nerves are sometimes attacked in tertiary syphilis as a true neuritis accompanied with evidences of neural degeneration. It may arise from a gummatous infiltration of the sheath, or from pressure of an exostosis as the nerve emerges from a bony canal. The sciatic nerve is frequently affected and this syphilitic sciatica may be most intense, causing in some instances contractures of the muscles and paralysis or paresis of the leg. Paralysis of the third cranial nerve is nearly always due to tertiary syphilis, either at the root or somewhere along its course. The two principal symptoms are diplopia and ptosis. Because of the dropping of the eyelid and the double vision the patient may have a staggering and uncertain gait. Optic neuritis, papillitis and choked disk when found upon ophthalmoscopic examination should always cause a suspicion of syphilis to be entertained.

The Treponema pallidum in the tertiary stage of cerebral syphilis may attack, by way of the meninges, the arteries, or may cause a primary degeneration in the brain substance itself. Not infrequently all three are affected either simultaneously or in the progress of the disease. In cerebral syphilis the base of the brain is attacked more frequently than the convexity. A basilar meningitis, due to a gummatous infiltration, may develop, or a basilar encephalomalacia due to gummatous infiltration of the arteries, or the two conditions combined may give rise to the symptoms. In these cases the cranial nerves are also in nearly every instance affected. If the lesion is focal some one symptom will usually stand out to the exclusion of others, whereas, if the process is diffuse the symptoms will be numerous. Cerebral syphilis usually begins with headache. Later, as the disease progresses mental apathy and dulness come on. This hebetude may pass into a stupor from which the patient cannot be aroused. Long before this, however, when the patient may not be complaining there may be observed rigidity of the pupils or one may be normal and the other widely dilated—inequality of the pupils. In addition to this there may be strabismus and anisocoria. In the early stages of cerebral syphilis the reflexes are likely to be exaggerated, later they are lost. These symptoms foretell either a developing psychosis or a suddenly appearing coma. Hence, basilar cerebral syphilis is a very important entity calling for prompt and energetic therapeutic measures. Not a few of these cases recover, especially if the symptoms occur within ten years of the initial lesion, and those cases offer the best prognosis in which coma develops rather than a psychosis. Should the condition develop into a psychosis it may imitate almost any—paranoia, dementia, manic-depressive insanity.

Syphilis of the vertex differs somewhat in its symptomatology from basilar syphilis because of the anatomic situation of the two inflammatory processes. However, in not a few cases it is extremely difficult to determine whether certain symptoms are due to disease of the convexity or the base, or if both are involved. Not infrequently when the vertex is involved the symptoms are general rather than local. This is because there are no large vessels on the vertex and none of the cranial nerves originate therefrom. Syphilis of the vertex can, however, present certain symptoms which may be regarded as characteristic. These are symptoms of irritation and paralysis caused by involvement of the motor cortical centers which are manifest as convulsions and paresis of various voluntary muscles. As in basilar syphilitic disease there is intense cephalagia and the powers of comprehension are decreased. The gait and other movements are slow and clumsy. The patient may stagger like a drunken man. In this stage the clinical picture very strongly suggests brain tumor—syphilitic or otherwise. Again, the process from the beginning may be acute. Delirium may come on, later developing into a comatose state. An important generalization in both syphilis of the base and of the vertex is that in cortical lesions thus developing these never occur alone, but are always accompanied with lesions elsewhere in the body. In many of these cases there may be a diffuse meningo-encephalitis which may be the basis of paresis, yet the process may stop short at that and not develop the latter. Jelliffe states that syphilitic meningo-encephalitis may so closely simulate paresis that it is well nigh impossible to differentiate between the two. Our principal resource in differential diagnosis is to be found in the four reactions of Nonne. If these are present it is paresis; if they are absent it is cerebral syphilis. The significance of these tests will be discussed in detail in the chapter on the Serology of Syphilis.

Cerebral syphilis caused by vascular changes, includes that caused by the large and the small vessels. Changes in the small vessels tends to produce paralyses—hemplegias and monoplegias. When the large vessels are affected a condition closely simulating paresis may arise.

Cerebral syphilis usually develops within a comparatively short time after the affection, but, except in extremely rare instances it always partakes of the nature of a tertiary lesion. In this respect cerebral syphilis contrasts greatly with paresis which does not appear for many years after the initial lesion and is a disease of very slow development. Cerebral syphilis may respond to treatment with almost miraculous promptitude, yet I am in accord with Collins that no matter how complete the clinical cure may be, these patients are never the same as they were before—the "syphilitic scars of the spirit" always remain.

Paresis or general paralysis of the insane (G. P. I.) may be termed the culmination of nervous syphilis. So important is it and so varied in its onset and development that I have reserved it for a separate chapter.

Hysteria and neurasthenia are sometimes observed in tertiary syphilis as due to the disease; as a rule, however, these neuroses are more frequently encountered in the secondary stage, and are due to the toxemia of the more recent and active infection.

Epilepsy.—A frequent form of nervous syphilis due to a circumscribed cortical irritation is epilepsy. It differs from the idiopathic type in that it begins at a much later period of life. In fact epilepsy, developing after thirty years of age, should always cause syphilis to be suspected. Syphilitic epilepsy differs also from the idiopathic form in that it is usually amenable to specific treatment. Also, the *aura* concomitant with idiopathic epilepsy is nearly always absent. Generalized convulsions are rare unless they are those which usher in paresis. They are almost invariably of the Jacksonian type. The syndrome in which there is giddiness and impaired power of orientation, commonly known as Ménière's disease may be caused by tertiary syphilis of the labyrinth. It is rarely encountered and is really due to an osteitis of the bones comprising the inner ear, yet the symptoms are such that they may suggest involvement of the cerebral membranes.

Strange as it may seem, and contrary to general opinion, gumma of the brain is comparatively rare. According to Larkin, it occurs twenty times less frequently than gummata of the other viscera. It is sometimes extremely difficult to distinguish between gumma and brain tumor, the symptoms being much alike—increased intracranial pressure, headache, giddiness, focal vomiting, somnolency, choked disk.

CHAPTER XIII.

LATE SYPHILITIC DERMATOSES.

The cutaneous lesions occurring in the tertiary stage of syphilis are different from those of the secondary stage. The lesions of the tertiary stage are more chronic, that is they are of slower evolution than those of the secondary stage; they are also more destructive, that is the tendency to ulceration is much greater; except in rare instances they are not symmetrical; that is, they are not evenly distributed over the body—they are placed irregularly and without order; they are also fewer in number, that is, their eruptive incidence is never generalized. They also dip deeper into the layers

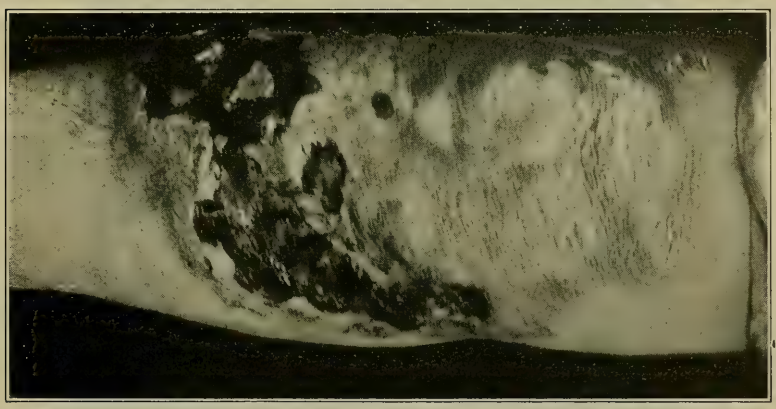


Fig. 34.—Serpiginous gummatous ulceration. (Courtesy of Dr. M. B. Parounagian.)

of the skin than the secondary lesions which are always more or less superficial. The scars left by them are permanent, the dyschromias are very frequently so; both of which testify to their chronicity and destructiveness. They are frequently influenced in their appearance by extraneous causes, that is, irritation has more to do with their appearance than it has to do with the lesions of the secondary stage which are almost, if not entirely, due to the intensity of the general toxemia.

The Gumma.—As in tertiary manifestations, elsewhere the characteristic cutaneous lesion is the gumma. If this is small it

is called a nodule; if it is smaller still and inclined to be conical and to project above the level of the skin it is called a tubercle. By some, however, the tubercle is considered to be a more than usually condensed and elevated papule. In passing, I would say that I am in accord with Fordyce that the differences existing between the cutaneous lesions of late syphilis are of degree rather than of kind. There are other lesions, however, which are distinctive of the tertiary stage of syphilis, but these also have a characteristic in common with the gumma—they ulcerate. These lesions are

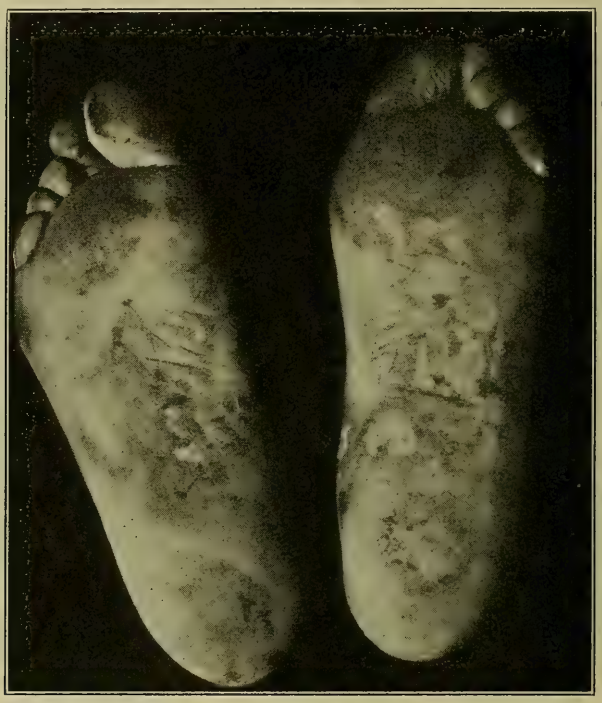


Fig. 35.—Plantar syphilide. (Courtesy of Dr. M. B. Parounagian.)

more superficial than the gumma and thus are more like the lesions of the secondary stage but they differ from these in their extreme chronicity. The names applied to these lesions are descriptive of their configuration or location, as squamous or serpiginous, or palmar or plantar syphilides. A lesion which is a very common cutaneous manifestation of tertiary syphilis is rupia, which is derived from a Greek word meaning filth. Some lesions also are named after the dermatosis they more or less closely simulate, and these will be described in their proper place.

Cutaneous Gummata.—The histology of a gumma of the skin or of the tissues immediately beneath does not differ in detail from a gumma that occurs elsewhere. Since the formation of these new-growths has already been discussed in the chapter on Pathology,

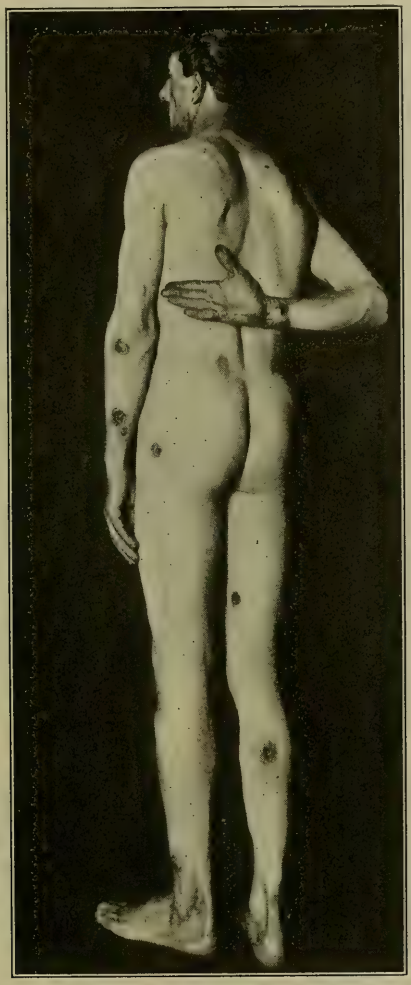


FIG. 36.—Ecthyma. (Courtesy of Dr. M. B. Parounagian.)

I will not burden the reader by repeating it here; rather will I hasten to describe its clinical appearance and the dermatologic processes with which it may be confused. As I have already stated the nodule and the gumma are the same except as to size.

A description of one will, therefore, suffice for the other. A cutaneous gumma may vary in size from a pigeon's egg to a hen's egg. Gummata of larger size than this have been reported but I have never seen one—the possibility of such, however, I do not deny. It begins

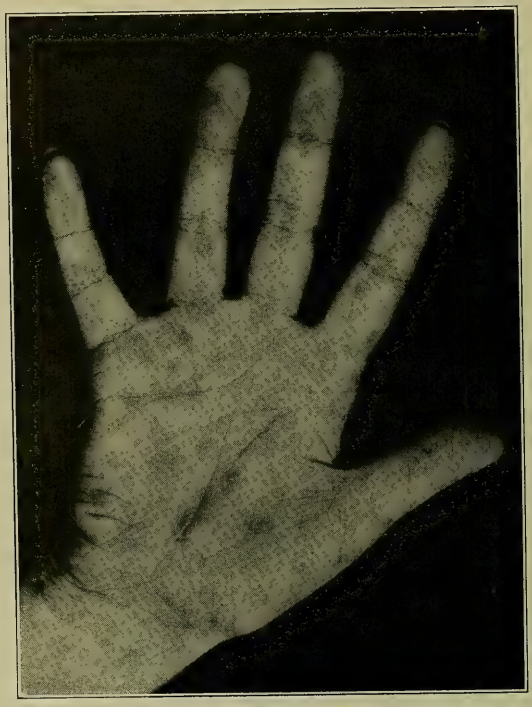


FIG. 37.—Macular palmar syphilide. (Courtesy of Dr. M. B. Parounagian.)

FIG. 38.—Ulcerating nodular syphilide. (Courtesy of Dr. M. B. Parounagian.)

as a small, more or less circumscribed infiltration beneath the skin, which at this stage of its development is not reddened or infiltrated. It rapidly increases in size, however, and soon feels like a small cyst under the skin which has by this time become reddened and sometimes slightly puckered or retracted. If the process is allowed to continue the skin over the gumma breaks down and an ulcer forms with sharply defined edges and perpendicular sides. The floor of the ulcer is covered with a grayish slough, from which arises a foul, sanious discharge, which may overflow and irritate the surrounding integument. This is a gummatous ulcer and as such may occur anywhere on the cutaneous surface. If it occurs over a bone, as on the calvarium, or in the nostril near the bony septum the ulcerative process may extend to the bone itself and cause an osteomyelitis with consequent destruction of the bone in the immediate vicinity of the gumma. Not infrequently these cutaneous gummata occur on the leg, and if they occur below the knee

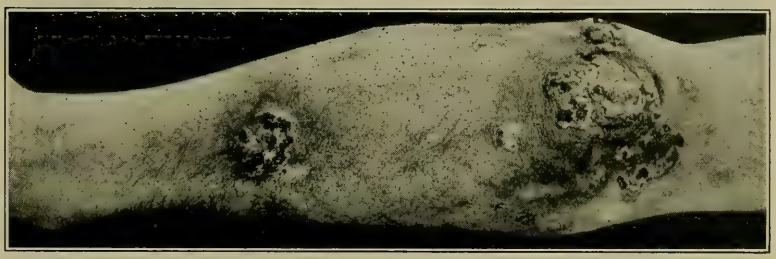


Fig. 39.—Nodular syphiloderm. (Courtesy of Dr. M. B. Parounagian.)

may be mistaken for a varicose ulcer, especially if the patient is a middle-aged obese man or woman with varicose veins. This likeness to a varicose ulcer is increased if the gumma has persisted for some time and an eczema has developed around it. Varicose ulcers, however, usually occur on the leg immediately above the ankle and are almost invariably accompanied with pes planus or flat foot. A serologic test may be necessary to determine in many instances whether an ulcer of the leg is syphilitic or due to varicose veins. A gumma occurring on the face may be mistaken for epithelioma and frequently the resemblance is so close that resort must be had to the Wassermann test. The gumma, however, is painless, or if pain is present it is by no means marked; sharp, shooting pains are always present in epithelioma; there is no glandular enlargement in the vicinity of a gumma; the glands near an epithelioma are always enlarged; a gumma develops rapidly from a subcutaneous nodule or cyst; an epithelioma is of much

slower development and usually begins as a crack or fissure or as a small warty growth.

Tuberculosis.—Gummatous growths frequently occur in the tuberculous diathesis. When due to this cause they are of much slower evolution than the gummata due to syphilis and the overlying skin becomes red and inflamed much earlier in tuberculosis than in the syphilitic gumma. When ulceration occurs it is irregular in shape—rarely round or oval as in syphilitic gumma; there is also a tendency to sinus formation which is rare in syphilitic gumma. On the whole, tuberculous gummata are ragged in appearance, not so deep, with a tendency to sinus formation, and are usually found in the neighborhood of joints. They are most likely to occur in patients in whom there are the signs of tuberculosis

Fig. 40.—Palmar syphilide. (Courtesy of Dr. M. B. Parounagian.)

of the bones or glands and are rare in middle or late adult life when syphilitic gummata are most likely to occur. The discharge from the tuberculous gumma is thin and sanious like its syphilitic congener and the tubercle bacillus can nearly always be found therein and if used for inoculation purposes in guinea-pigs will nearly always cause tuberculosis to develop. This does not always happen, however, and failure of inoculation in these animals is not absolute evidence that the lesion is not tuberculous.

Sporotrichosis.—Sporotrichosis causes gummata to appear in the skin that most closely simulate those caused by syphilis. The new growths caused thereby, as in syphilis, may be single or multiple. They begin as painless nodules and soon soften and form abscesses. The margins of these ulcers are ragged and undermined and where

Fig. 41.—Palmar syphilide. (Courtesy of Dr. M. B. Parounagian.)

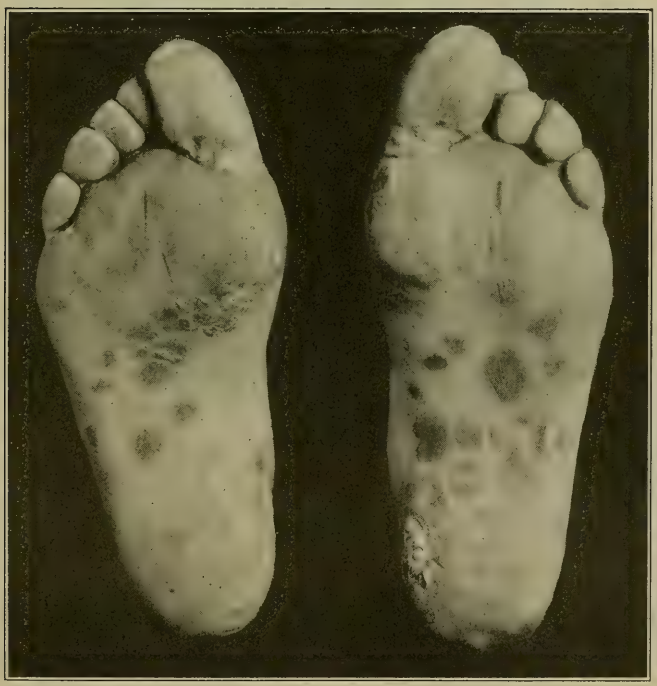


Fig. 42.—Plantar syphilide. (Courtesy of Dr. M. B. Parounagian.)

two or more ulcers are in proximity to each other the skin between them is deeply inflamed and pierced with several openings not unlike a carbuncle. In some instances papillomatous excrescences appear, not unlike framboesiform syphilides. Cicatrization may occur with persistence of the abscess under the skin. The lesions are also autoinoculable. These last two features are never present in syphilitic gummata. However, these lesions are often extremely difficult to differentiate from those caused by syphilis and in many instances the Wassermann test and the discovery of the fungi in material obtained from a lesion are the only means of differentiation.

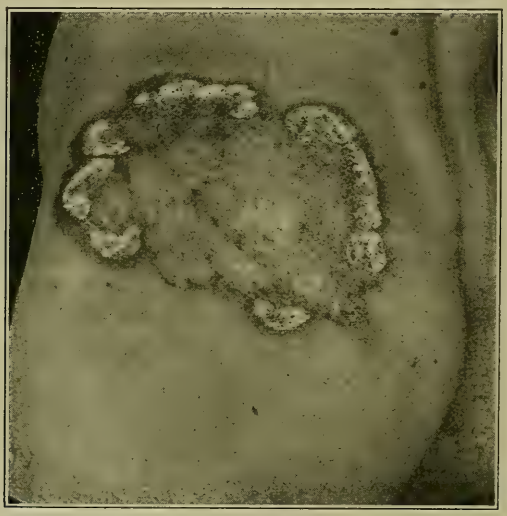


FIG. 43.—Tertiary serpiginous syphilide. (Courtesy of Dr. M. B. Parounagian.)

Actinomycosis.—Cutaneous actinomycosis may be mistaken for a syphilitic gumma. The cutaneous form of the disease usually attacks the integument of the face or neck. Nodular masses form which rapidly soften and break down and discharge through several openings a semipurulent material. The process is extremely chronic. The discovery of the ray fungus, which can nearly always be found in the discharge from the gummatous mass, will establish the diagnosis.

In some instances there is a gummatous infiltration of the skin, that is, the gummatous process instead of being a cyst-like growth is spread out superficially, so that when ulceration occurs the area of cutaneous destruction is much greater, but the depth of the ulceration is much less than when the process is circumscribed. This superficial gummatous ulceration may be of considerable

size and, while its contour is usually rounded or oval, it may be decidedly irregular. A seropurulent fluid exudes from the unhealthy granulations forming the floor of the ulcer which dries into a blackish-red crust.

Cutaneous gummata usually heal promptly under arsphenamine treatment. If the growth has not broken down however, and is soft, I am in the habit of evacuating the gummy contents of the mass and following the arsphenamine with massive doses of potas-

FIG. 44.—Tertiary serpiginous syphilide. (Courtesy of Dr. M. B. Parounagian.)

sium iodide. It has been my experience that their disappearance is hastened by this method, more so than when arsphenamine alone is administered. In some instances cutaneous gummata resolve without treatment, that is, they reach a certain size, do not break down and gradually disappear by absorption. The scar left by a gumma is usually comparatively small for the size of the ulcer. It is white in the center, slightly depressed and surrounded by a pigmented border.

Nodular Syphilide.—The nodular syphilide is a small gumma and its pathologic evolution is identical with the growths of larger size. They vary in size from a pea to an almond. They are round or oval in shape and are sharply circumscribed and the skin above may be normal or slightly reddened. They are painless, or only slightly tender, when pressed upon. They occur most frequently on the extremities, but are not infrequently found elsewhere. They are irregular in the points of their appearance, but when present are always more numerous than gummata. When ulceration occurs they are identical in appearance with gummata except in size. In rare instances when these nodules ulcerate the granulations, forming the sides and floor of the ulcer, hypertrophy, which gives them the aspect of red papillomatous growths from which exudes a muco-purulent discharge. Because of their close resemblance to the characteristic lesions of framboesia or yaws they are called framboesiform syphilides.

Nodular syphilides resemble to some extent the nodules observed in other dermatoses—notably, leprosy and the subcutaneous new formations known as sarcoids. As a rule, however, there is no difficulty in distinguishing between these and nodular syphilides. In the United States, except in Louisiana and in some of our Island possessions, leprosy is an extremely rare disease—a medical curiosity as it were. For that reason it can nearly always be ruled out. It must not be forgotten, however, that a positive Wassermann reaction is sometimes obtained in nodular or tubercular leprosy. The nodules of leprosy are usually associated with the tubercles which, when present in a case that is sufficiently advanced, are characteristic enough to enable a differential diagnosis to be made. They occur as deeply subcutaneous nodules that can often only be felt after a careful search, as they barely raise the skin. They are found most frequently on the buttocks, the back and the outer aspect of the legs and arms. They are often found in the lobules of the ears—and these auricular nodosities, I might add in passing, are, when found, extremely suggestive of leprosy.

Sarcoids.—Sarcoids are multiple subcutaneous nodules of slow growth and without pain and are usually arranged in symmetrical groups. They rarely, if ever, ulcerate and are found on the thorax following the course of the ribs, the anterior aspect of the thighs and the abdomen. They elevate the skin but slightly, which may be normal or of a dull-red color. If there is any doubt a Wassermann reaction will determine the diagnosis. While not related to syphilis in any way, these lesions rapidly yield to arsphenamine and mercury.

Tubercular Syphilides.—Tubercular syphilides, when they occur in the secondary stage, are usually condensed and solidified papules,

but in the tertiary stage I am inclined to classify them in so far as their pathologic formation is concerned as minute gummata. They appear as round or conical elevations projecting from the skin, firm and smooth and of a dark-red or coppery color. They are rarely, if ever, disseminated but occur in groups of circular or serpiginous outline. They are extremely indolent in their course, although spontaneous evolution sometimes occurs. When they disappear they invariably leave a pigmentation. Tertiary tubercular syphilides nearly always ulcerate. The ulceration occurring in these lesions is not as deep as that which occurs in gummata or nodules. When an aggregation of tubercles in a circular or gyrate arrangement, ulcerate, ulceration may be present at one part while healing is going on at another. Thus, a syphilitic nodule, which may have formed the center of a circle of satellite tubercles, may have ulcerated and healed as a white, atrophic scar while the circle of tubercles may be in an active stage of ulceration, and may be covered with dirty yellow crusts. It is this tendency to extend peripherally that gives rise to the term serpiginous which thus describes a method of development rather than a type of lesion. This serpiginous form of ulceration is pathognomonic of syphilis. In some instances, particularly on the face the tubercles may be grouped in a corymbiform arrangement which bears a very close resemblance to lupus serpiginosus.

Rupia.—A cutaneous lesion of comparative frequent occurrence in late syphilis, usually in those who are cachectic from any cause, is rupia. The word rupia is of Greek origin and means dirt and is applied to these lesions because of their dirty appearance, or, as was once erroneously supposed, that they arose from personal uncleanliness. It never occurs in congenital syphilis. Rupia usually arises from a group of tubercles that have coalesced and ulcerated. The exudate from the ulceration forms a yellowish or blackish crust which covers the ulcer; exudation continues beneath this, and also dries; the continuation of this exudation and drying thereof and the superimposing of these successive layers of crusts one above the other gives the lesion the characteristic laminated appearance which is peculiar to it. Since the lesion extends by peripheral ulceration, each new crust formed is larger than the preceding so that the general appearance of the lesion is that of a blackened oyster shell or a horny growth or keratoma projecting from the skin for a centimeter or more. If this accumulation of crusts or scabs is removed an unhealthy ulcerating surface will be exposed. Rupia sometimes occurs in early syphilis when the disease is severe and it then arises from an ecthymatous syphilide or a papule that has become pustular. These lesions are usually surrounded by an inflammatory collar, but in the tertiary lesions this

encircling inflammation may be wanting. In some instances only one or two crusts may form so that the characteristic laminated

Fig. 45.—Rupia.

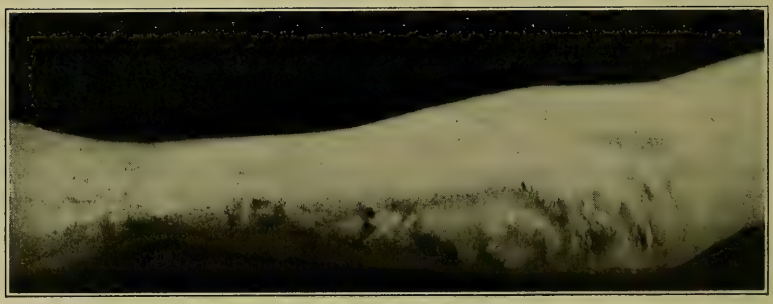


Fig. 46.—Rupia.

crustaceous appearance is wanting. In size the crusts may vary from a dime to a dollar. They are not, as a rule, numerous, unless of small size and even then they rarely number more than a dozen. The small rupia are usually seen on the face and on the inner and outer surfaces of the forearms. The large rupia are most frequently met

FIG. 47.—Rupia.

with on the outer aspect of the thighs and legs. When healed the lesions leave white atrophic scars surrounded by more or less pigmentation. The diagnosis of rupia is not difficult as there is no other dermatologic lesion that resembles it sufficiently to create any doubt as to its origin. It is not only characteristic; it is pathognomonic of syphilis.

In the late as well as in the early stage of syphilis, as I have already described, squamous syphilides may appear on the palmar or plantar surfaces. Frequently the lesions that appear late—sometimes many years after the initial lesion—cannot be distinguished from the early lesions. For this reason Fournier has described them as "delayed secondary manifestations." The tertiary lesions, however, are usually unilateral, that is, the palm or sole of one hand or foot is involved; the lesions show as discrete red spots deeply imbedded in the skin and are frequently hyperkeratotic, that is, they look like horny nodules or "corns." There is also less tendency to scale or desquamate in the tertiary lesions, although scaling is never entirely absent. Surrounding the squamous area, which may be small or so large as to include the entire palm or sole—minute tubercles are sometimes seen. Cracks and fissures following the palmar or plantar lines are sometimes present. These lesions may be mistaken for eczema or psoriasis, but a careful examination will usually reveal the differences whereby a diagnosis can be made without having to resort to the Wassermann test which, however, should not be neglected in any event. Eczema is usually bilateral, whereas if the lesion is syphilitic it is usually unilateral, and if of the palm it is usually the right (being the one that is used the most). The syphilitic lesion is usually more circumscribed than eczema; its color is darker—the characteristic "coppery" hue of syphilis. The process is more active at the circumference than at the center if it is syphilitic. Also, the syphilide does not itch, whereas eczema always does. In this connection, however, I wish to say that the presence of itching does not necessarily preclude the lesion from being syphilitic as some text-books state, because not infrequently these palmar and plantar syphilides are associated with a secondary eczematization provoked by the syphilitic eruption. Psoriasis is more scaly than the syphilitic dermatosis and the psoriatic patches are also apt to be found on the wrists and ankles and elsewhere on the body; whereas palmar or plantar syphilides may be the only cutaneous manifestations of the disease.

These lesions of the palms and soles are usually very chronic when seen by the physician. In order to cure them promptly local measures must be used in conjunction with the constitutional treatment. If there is much callus, this must be softened and removed, for which purpose green soap or Lassar's paste should be used, preferably by means of a plaster continuously applied for twenty-four or forty-eight hours, or applied for several successive nights and removed during the day. When the horny layer has been removed a plaster composed of equal parts of mercury ointment and zinc oxide ointment should be applied in a similar manner for

about a week when it will be found that the lesions will have entirely disappeared.

Urticaria.—In late as well as in early syphilis urticaria is sometimes observed. The urticaria of the late stage does not differ from that observed in secondary syphilis.

Roseola.—A rare and peculiar phenomenon observed in tertiary syphilis is a recurrent macular eruption, the so-called tertiary erythema or roseola. These recurrent macules are larger, paler and less numerous than those of the secondary stage. Strange to say they are most frequently observed in cases that have received energetic treatment. According to Darier they are "the attenuated equivalents of tuberculo-ulcerative syphilides."

Telangiectasis.—Stokes and also Ehrmann have called attention to telangiectasis or red patches irregularly scattered over the body, due to capillary dilatation similar to nevi or birth-marks. A dermatosis characterized by purpuric spots known as Majocchi's disease, or purpura annularis telangiectodes, is also in my opinion sometimes due to syphilis, either acquired or as a late congenital manifestation.

Elephantiasis.—Elephantiasis is sometimes caused by syphilis. The appearance of this monstrous dermatosis is so typical that I will not burden the reader by giving a detailed description of it. When due to syphilis it is caused by a gummatous infiltration of the lymphatics, or an obliterative endophlebitis—usually of the legs.

Raynaud's Disease.—Symmetrical gangrene, or Raynaud's disease, is sometimes due to syphilis. It is a rather infrequent condition and is most often seen in those of a neurotic tendency. It may be due to acquired syphilis, but in my opinion it is more likely to be a manifestation of late congenital syphilis. It occurs most frequently in young adults, especially those whose occupation entails exposure. The fingers are most frequently affected, then the feet, the tip of the nose and the ears—rarely, other parts of the body. The parts affected—as the fingers—are first pale and cold and then red and hot; that is, there is first an ischemia followed by a congestion. This may last for a few minutes or for several hours and is usually attended with painful tingling or burning sensation. These attacks may occur only at wide intervals or they may occur very frequently—every day or every few days. The attacks characterized by cyanosis as the predominating feature, if long continued, eventually cause gangrene of the parts affected. Blisters form and the skin beneath ulcerates—the gangrenous process is usually confined to the skin, but it may involve the deeper structures, including the bones. If gangrene does not follow the parts affected sooner or later show atrophic or sclerodermatous changes. The spasmodic character of the attacks point to changes in the vasodilators and

vasoconstrictors of the terminal veins and arteries; it is thus an angioneurosis, probably of central origin as Pusey believes, and with him I am in accord.

In all cases of Raynaud's disease syphilis should be suspected especially syphilitic involvement of the central nervous system. A serological test of the blood is, therefore, not sufficient, but the cerebrospinal fluid should invariably be examined as well.

When the attacks occur the parts should be rubbed with cracked ice in a towel—hot applications should not be used under any circumstances. As recommended by Raynaud the application of galvanism is of benefit. The part affected should be immersed in salt water and the negative pole placed therein, while the positive pole is applied to the spine. A current as strong as the patient can bear should be used, with frequent interruptions to cause contractions of the parts.

Phagedena.—Occasionally syphilitic lesions of the ulcerative type are attacked by phagedena, that is, by rapidly spreading destructive ulceration. The cause of phagedena is unknown as it occurs in the robust as well as in the debilitated. It is possible that it is due to a superadded infection or to an unaccountable lack of tissue resistance. It is quite possible that both of these supposed factors unite to produce it. In passing I might add, that while phagedena is usually a concomitant of syphilitic lesions it is not always so. Phagedena added to a syphilitic ulcer is sometimes horribly destructive, and in an incredibly short length of time. For that reason when it occurs it should be attacked without delay and in the most vigorous manner, leaving no means untried whereby its ravages may be stayed.

Arsphenamine should be used to the exclusion of mercury. It should be given intensively, and if the patient is debilitated rest and supportive treatment must be added thereto. Local treatment is imperative and consists of hot irrigations several times a day with solutions of potassium permanganate of a strength of 1 : 2000 or 1 : 3000; using several liters for each irrigation. Pouring tincture of iodine on the ulcer once a day sometimes arrests the progress of the phagedena. If this is done the ulcer should be surrounded with a dam of absorbent cotton impregnated with vaseline in order to protect the skin about the ulcer from the irritating effects of the iodine. If the ulceration is situated where it is possible for this to be done, immersion for several hours, or even all day, in a permanganate bath is very beneficial. Continuous irrigation with Carrel-Dakin solution, in theory (and, I have no doubt, in practice also, although I have never tried it) should be especially efficacious. The Paquelin cautery has been advised and may be tried, but personally I am not in favor of this measure. Hot air, with the

patient under general anesthesia, is recommended. A hot-air apparatus is not always obtainable, and for that reason I have found that pouring *boiling* water on the ulcer, care being taken to protect the surrounding parts, produces results equally as good. This method, which may seem heroic, as it doubtless is, was first used by Jeanel for the treatment of carbuncle many years ago. It has an equally prompt effect in limiting the progress of phagedena. Under no circumstances should powders or salves be applied.

The results of tertiary syphilides are dyschromias, atrophies, scars and keloids—the last especially frequent in negroes. These cutaneous sequelæ cannot be influenced by constitutional treatment and are in nearly every instance permanent.

Congenital Syphilis.—The later cutaneous manifestations of congenital syphilis are nearly always gummatous. In appearance and evolution they do not differ from similar lesions in the acquired form of the disease. Not infrequently late congenital syphilitic skin eruptions simulate very closely those caused by tuberculosis, especially some forms of lupus. Not only does late congenital syphilis resemble tuberculous dermatoses, but many other dermatoses of childhood, especially if chronic. For that reason all skin lesions that are rebellious to treatment in children under fifteen years of age should be subjected to a careful scrutiny for possible congenital syphilis.

CHAPTER XIV.

CONGENITAL SYPHILIS.

The terms congenital and hereditary are used interchangeably to denote that form of syphilis which is transmitted from parent to child. I am in accord with MacCallum that congenital is the better qualifying word in that the disease is not transmitted as a hereditary characteristic, but rather as an infection transmitted to the fetus during its development *in utero*.

Congenital syphilis differs in degree and not in kind from the acquired form. It is more intense. Congenital syphilis also differs in that it has no primary stage—the child being born with the symptoms of the secondary or tertiary stage fully developed. Syphilis can be transmitted to the offspring either by the father or mother or by both. It is more likely to be transmitted from the mother than from the father. If the parent's syphilis is tertiary it is quite possible that the child will escape the taint altogether. Also, if the mother is infected during the last six weeks of her pregnancy it is possible that the child may escape infection. As a result of syphilis in the mother abortion may occur, or there may be the discharge of a macerated fetus before term, or a still-born child at term, or a child born alive prematurely or at term and surviving only a few hours, or a seemingly healthy child may be born which later displays the symptoms of congenital syphilis, or a healthy child may be born which remains so for many years and then at puberty or later display symptoms of syphilis. In the vast majority of cases the mother shows no clinical evidences of the disease, although in the father they may be very plain. It is also possible that a child may be born apparently healthy and remain so, whose parents, either one or both, are patently syphilitic. These apparently healthy children born of parents, one or both of whom are syphilitic, will in almost every instance show a positive Wassermann reaction in the blood. The observations of Mangiagalli show that when both parents are syphilitic the child will be a congenital syphilitic in about 75 per cent; when the mother alone is syphilitic the child will be syphilitic in about 60 per cent; when the father alone is syphilitic the child will be so in from 10 to 20 per cent of all cases.

Since the introduction of the Wassermann test a clearer insight as to the incidence of syphilis in both mother and child is possible;

also, we now know the reason of the mechanism of Colles' and Profeta's laws, which before were wrapped in mystery. Colles and Baume and Profeta reduced to aphorismic formulas the facts observed by them which could not be explained until the advent of the Wassermann reaction.

Colles' Law.—In 1837 Colles made the following statement: "A child born of a mother who is without obvious symptoms and which, without being exposed to any infection subsequent to its birth, shows the disease when a few weeks old, this infant will infect the most healthy nurse, whether she suckle it, or merely handle and dress it, and yet this child is never known to infect its own mother, even though she suckle it while it has venereal ulcers of the lip and tongue."

Profeta's Law.—In 1865 Profeta observed that: "A healthy child born of a syphilitic mother could be suckled by her or by a syphilitic wet nurse with impunity."

We know now the reason for these apparent inconsistencies. We know that the apparently healthy mother is a latent or a symptomatic syphilitic and that the apparently healthy child is the same; neither can acquire syphilis from the other because they both already have it.

The source of transmission, either by the father or by the mother, has no influence on the symptoms of the disease. The earlier the manifestations of the disease in either parent the more severe the symptoms are apt to be in the child. As the disease progresses in point of time, that is the older the infection becomes, its transmissive incidence is correspondingly diminished until it almost, if not entirely, disappears. After the tenth year transmission to the offspring is comparatively rare. However, I would qualify this statement by saying that exceptions occur with sufficient frequency that vigilance to prevent such a misfortune should not be relaxed where one or both parents are known to be syphilitic.

The lesions of congenital syphilis are those of the secondary and teritary stages in the acquired form of the disease. In congenital syphilis there is always an excess of the fibrous elements over the glandular which in a measure accounts for the congenital weakness—the "inaptitude for life," as Fournier expressed it—of such children.

Symptoms.—The symptoms of congenital syphilis are rarely present at birth. Indeed, many infants, which later develop all of the typical symptoms of congenital syphilis, at birth appear remarkably healthy and well nourished. The great French syphilologist, Diday, makes mention of the "look of the little old man," and says that the syphilitic infant can be discerned almost as it emerges from its mother's womb, but this is true only in a comparatively small number of cases. Undoubtedly some syphilitic

infants show at birth unmistakable signs of the disease which usually takes the form of an eruption of pustules, papules or bullæ; but these infants almost invariably die within a few days, and before much marasmic wasting can take place. It is true that in many instances a profound marasmus rapidly supervenes which gives the infant the appearance so graphically described by Diday, but it must also be remembered that in far the greater number of cases local symptoms only are present without any other sign of the constitutional dyscrasia.

Snuffles.—One of the earliest, most frequent and most noticeable symptom of congenital syphilis is the coryza termed by the laity "snuffles," due to swelling of the mucosa, especially of the inferior turbinates. About the time of the appearance of the "snuffles" or shortly after, it is also noted that the infant's cry becomes rather hoarse—the *vox syphilitica*. It is the snuffling nose and the hoarse croaking cry that helps to confirm the opinion of the mother and others that the infant has a "cold." Should this inflammatory process of the nasal mucous membrane continue the nasal bones will in time be attacked and the typical saddle nose, pathognomonic of congenital syphilis will result. The swelling of the nasal mucosa may make breathing difficult and thus interfere with the infant's nursing, and inanition due to lack of nourishment will be added to the already existing syphilitic dyscrasia. Frequently, following the coryza a rash appears about the buttocks, or upon the trunk and legs, rarely upon the face. When the infant's abdomen is palpated the spleen is found to be enlarged and the liver markedly so. In male infants the testicles are larger and harder than normal. *Pseudoparalysis syphilitica* of Wegner, as a rule, comes on rapidly in these cases. This is really an epiphysitis of the bones of the extremities, making it impossible for the infant to move its arms or legs. If the infection is severe, blebs, or bullæ may form on the soles or palms or on other parts of the body. At first filled with clear fluid, these blebs soon become infected and a general sepsis ensues, from which the infant frequently does not survive. This *pemphigus syphilitica* must, however, be differentiated from the pemphigus neonatorum, frequently seen in ill-fed marasmic infants due rather to low tissue resistance than to a specific disease such as syphilis. Fissures and mucous patches may be present about the anus and lips, on the tongue and the buccal mucous membrane. These lesions are highly infectious as many have found to their cost. It is these fissures or rhagades at the angles of the mouth which after healing show as radiating scars in after years, and as such are characteristic of congenital syphilis. Gummata of the skin or "syphilitic furuncles" are not uncommon. They begin as a slight hardening of the skin which is also slightly raised and red.

This spot of induration rapidly turns to a deep purple color and softens in the center and ulcerates. Should the gumma be opened, under the impression that it is a furuncle, a scanty amount of thin, sanious pus will exude.

Pharyngitis.—Chronic catarrhal pharyngitis is almost always present in the early phase of congenital syphilis and unless checked may go on to superficial or deep ulceration and extend to the tonsils and fauces. Perforation of the soft palate may occur. These lesions are also frequently accompanied with otitis media. Iritis and choroiditis may occur in the first year of life due to congenital syphilis but, as a rule, ocular complications are rarely seen so early. The bones of the skull may be the seat of gummatous periostitis which later consolidate and give the cranium a "knobby" appearance. It is these nodes on the frontal bone which gives the characteristic "Olympian forehead" mentioned by Fournier as frequently seen in children who in infancy suffered with congenital syphilis. When occurring on the vertex the so-called "hot-cross-bun" effect is sometimes observed. The bones of the calvarium may, on the other hand, become abnormally thin and the condition known as craniotabes will be found. These osseous lesions of the skull may be mistaken for rachitis, but the signs of syphilis in other parts of the body will usually clear the diagnosis. Strange as it may seem, the hair in syphilitic infants may be very abundant—the "syphilitic wig;" the contrary may also exist—hair may be entirely wanting. The lymphatic glands, the enlargement of which is so characteristic of acquired syphilis in the early stage, is not noticeable in infants with congenital syphilis, and in older children it is not marked.

Hemorrhage.—A condition that frequently supervenes in newborn syphilitic infants and which is nearly always fatal is *syphilis hæmorrhagica neonatorum.* The hemorrhage may be subcutaneous or from the mucous surfaces; most frequently it is from the navel.

In the severe cases such as I have described as the local symptoms develop the infant soon becomes marasmic. It steadily and rapidly loses weight and becomes profoundly anemic. It cries continually—more so at night. The little body wastes until it is but a bag of bones with a drawn and wrinkled face, sallow and blotchy—a pitiful travesty of all that a healthy infant should be. Unless the toxemia is allayed by treatment, death almost invariably occurs from malnutrition, pneumonia or diarrhea.

Hutchinson's Teeth.—Should the child survive dentition it will be observed that the temporary teeth are prone to decay, but are otherwise not distinctive of the disease. When the permanent teeth erupt in many instances they present certain characteristics which are pathognomonic of congenital syphilis. The upper

central incisors give this information. They are peg shaped, short and narrower above than below where they emerge from the gums. On the cutting edge is a notch where the dentine is exposed. This notch may be shallow or deep and to teeth so affected has been given the name of Hutchinson's teeth after the English syphilologist, Jonathan Hutchinson, who first described them as a sign of congenital syphilis. Not every congenital syphilitic has Hutchinson's teeth however. It is now asserted that these characteristically

Fig. 48—Hutchinson's Teeth.

notched teeth may be observed in other conditions than congenital syphilis. But be this as it may, their presence should always arouse a suspicion of congenital syphilis. In addition to Hutchinson's teeth there are other dental abnormalities which are sometimes associated with congenital syphilis. These are horizontal grooves on the teeth, dental infantilism, cup-shaped erosions on the deciduous molars and cuspal atrophy of the first permanent molars. Recently attention has been called to other dental anomalies which heretofore have not been considered of diagnostic import in congenital syphilis. These are abnormal spacing of the upper central

Fig. 49—Hutchinson's Teeth.

incisors, which are long and cylindrical in shape, mammillary eminence or an accessory cusp on the lingual side of the first upper molar. It must always be remembered in this connection that these dental stigmata, as it were, are frequently encountered in congenital syphilis; they are also encountered quite frequently in children who are entirely free from the taint. Their presence, therefore, while probably significant, should not be accepted without proper reservation.

Internal Organs.—The internal organs are also affected by the disease, most of which have their beginning before birth. Endarteritis is sometimes noted, although in congenital syphilis the vessels are less frequently involved than in the acquired disease. Shortly after birth the infant may succumb to a pneumonia which is distinctly syphilitic. Or later the infant's life may be terminated by a chronic interstitial pneumonia, or gummata may form in the lungs which may soften as in tubercle and form cavities. Interstitial or gummatous hepatitis may occur—usually the interstitial. A similar process may occur in the kidneys, or the kidneys may develop a parenchymatous inflammation. The symptom of paroxysmal hematuria—not to be confused with Winckel's disease—is strongly indicative of congenital syphilis. Interstitial changes in the suprarenals, or the pancreas, causing the so-called juvenile diabetes, may also occur.

Between the ages of five and fifteen years an interstitial keratitis, which usually affects first one eye and then the other, frequently occurs. It may persist for months in spite of treatment. Eventually it clears up, but not without opacities which interfere with vision and which can be regarded as strongly significant of a former syphilitic process. During this period deafness may come on. The loss of hearing is rapid and complete and is not amenable to treatment. In the early years of childhood gummatous ulceration, as in the tertiary syphilis of adults, may occur. Chronic periostitis of the tibiæ, producing the "sabre shins," observed in old adult syphilitics, and chronic synovitis with effusion, particularly of the joints of the fingers, are among some of the lesions which may be observed.

Nervous Lesions.—In infancy—that is, within the first two years of life—nervous lesions are rarely encountered with the exception of hydrocephalus which is almost invariably of syphilitic origin. After the fourth year or at the beginning of adolescence the cerebral membranes may become implicated and mental deterioration supervene—juvenile paresis. The cord and its membranes may be the seat of first a gummatous and later a degenerative process and the child may develop the symptoms of locomotor ataxia—Friedreich's ataxia, as the congenital form of juvenile tabes is known. Syphilis, in my opinion, is a very frequent cause of idiocy and imbecility, weak-mindedness, and all other forms of mental and moral degeneration observed in children and young adults. Truly these children suffer for the sins of their parents.

Children with congenital syphilis, if they weather the pathologic storms of infancy, rarely thrive. They are almost without exception thin, undersized, anemic and of slow growth. Rarely do they reach the full measure of a man physically or mentally. They

carry the stigmata of their inheritance through life. For, congenital syphilis nearly always leaves its mark. Its taint cannot be hidden, but stands forth plainly so that he who runs may read.

Diagnosis.—The clinical recognition of congenital syphilis in infants, particularly if the disease is active, is usually not difficult. Examine for a rash, especially about the buttocks; for ulceration about the anus, in the mouth, between the toes and behind the ears. In older children look for radiating scars at the angles of the mouth; examine the nose and throat for present ulcerations of the scars and deformities resulting therefrom; examine the teeth for dental stigmata; the bones, especially the tibiæ and the cranial bones, observe the general contour of the cranium; search for the scars and remaining discoloration of cutaneous gummata; examine the eyes for opacities indicating a former keratitis or iritis; note if deafness is present. In very few cases are all of these manifestations of congenital syphilis apparent. There may not be more than one or two; but even if one is found it is wise to take a Wassermann test of the blood. After the eighteenth year, however, the Wassermann is frequently negative even if the signs of congenital syphilis are plainly evident. In examining older children or young adults it is wise to remember Hutchinson's triad, that is, notched teeth, corneal opacities and deafness; if these three are present it is almost certain that the patient has, or has had, congenital syphilis.

Delayed Hereditary Syphilis.—This chapter would not be complete without discussing *syphilis hereditaria tarda*, or delayed hereditary syphilis, to translate it literally. By this is meant congenital syphilis that skips infancy and early childhood and appears either at puberty or in early adult life. It is possible, I may say, that this non-appearance in infancy is not absolute, in that there may have been symptoms which were either overlooked or else wrongly diagnosed. *Syphilis hereditaria tarda* may appear after the third year or as late as the thirtieth year. These cases of delayed congenital syphilis sometimes present the most abstruse problems in diagnosis, as they are very often occult to a high degree in so far as syphilis is concerned. As in acquired syphilis, the nervous system is very frequently selected for attack. Headache, persistent and severe, and insomnia if appearing at or shortly after puberty and if eyestrain and overstudy can be eliminated, should cause the physician to think of late congenital syphilis. In late congenital syphilis, as Fournier says, the brain may be attacked "quickly and severely." This means that focal epilepsy or hemiplegia may appear without warning; or the ordinary petit mal, or grand mal, with generalized convulsions may appear. Hemiplegia, occurring in youthful persons in whom no history of acquired

syphilis can be obtained, should cause a search for congenital syphilis to be made. The same is true of paralysis of one or more of the cranial nerves. Late congenital syphilis may also cause tabes or paresis, but in these cases other evidences of the congenital disease are rarely if ever absent. Such of these evidences as may be called dystrophies, I have reserved for a separate chapter.

It may be said that in a general way, all congenital syphilitics are more or less predisposed to organic and functional neuroses. They are more apt to develop infantile paralysis than other children. They are also inclined to neurasthenia, hypochondria, melancholia and to obsessions and phobias. Hysteria develops readily in this class of patients. In other words, acquired syphilis in the parents breeds degeneracy in the children.

Next in frequency to lesions of the nervous system are gummata of the skin and viscera. I am convinced that many cases of so-called "scrofula," as it was termed by the older writers is not tuberculosis at all, but late congenital syphilis. This is exemplified by many cases of lupus erythematosus and enlarged and ulcerated lymph nodes having been proved by the serologic test now in use to be syphilitic. Palmar and plantar syphilides may occur which differ not at all from those seen in acquired syphilis. Gummatous lesions elsewhere on the cutaneous surface occur. Osseous lesions are also represented in many forms; joint affections—syphilitic white swelling and chronic deforming arthritis, loose joints, characterized by habitual dislocations, lesions of the joints which cannot be differentiated clinically from those caused by the tubercle bacillus.

Valvular disease of the heart and aortic aneurysm are sometimes due to delayed congenital syphilis. The liver, spleen and kidneys may undergo cirrhotic changes or be the seat of gummata.

Only about 25 per cent of the offspring of congenital syphilitics survive, and females who show evidences of having had it are rather prone to lose the product of conception even if married to healthy men.

That congenital syphilitics can in turn give birth to children also congenitally syphilitic, I believe. This phase of congenital syphilis is discussed at length elsewhere in this book. It is also taught that congenital syphilitics cannot contract the disease anew. This I deny. The binary form of syphilis, as described by Tarnowsky, while not often encountered, is still, in my opinion, a fact that admits of no denial.

CHAPTER XV.

THE PROGNOSIS OF SYPHILIS.

If we examine the opinions expressed by syphilologists and internists in the past as to the curability of syphilis it will be found that the consensus of opinion was that syphilis was an incurable disease. This, of course, did not apply to the local external lesions which, except to the discerning few, comprised in the minds of most of them the principal manifestations of the disease. The grave visceropathies, neuropathies and psychopathies, which we now know to be absolutely syphilitic, were then either denied such origin or else were referred to as parasyphilitic or metasyphilitic, according as the author followed the French or German nomenclature. In those days—and they were not so very long ago—the cause of syphilis was alluded to as the "virus" and many and fantastic were the theories advanced as to the nature of it. The aphorism "Once syphilitic, always syphilitic" was then accepted as a fact by the majority of physicians—and is yet by some. The late Hayes Agnew, the famous surgeon of a generation ago, aptly expressed the view then current when he said that the man who has syphilis will have it all his life and his ghost will have it when he is dead. Fournier, who after Ricord was the greatest syphilologist of his time, voiced this widely held opinion in the now classic phrase: "Syphilis does not die, it only sleeps."

When we consider that the specifics—mercury and potassium iodide—were in most instances given only by mouth, except in rare instances when mercury was administered by inunction, fumigation or injection—the last timidly and tentatively if the reader will consult the text-books of the time—it can be readily appreciated why Agnew and Fournier believed the infection to be ineradicable. In the light of present knowledge we now know how few must have been the cures—by that I mean the complete sterilization of the body to the infecting organisms—in those days. The discovery of the Treponema pallidum, the Wassermann reaction and arsphenamine, brought about a revolution in our ideas of the pathology, the treatment and the prognosis of syphilis. Since that time—and all three of these epoch-making discoveries have been made within the last fifteen years—our knowledge of syphilis is no longer empiric, but rests upon a basis of scientific facts. It

is from this modern viewpoint that I propose to discuss the prognosis of syphilis.

I am firmly convinced that syphilis, as it now exists, differs considerably from the syphilis of former times. This evolution has been going on for many ages but it is only now becoming apparent. It is impossible to determine with any degree of accuracy just how and why this change has taken place, sufficient to say that it has. Civilization and syphilization, as Neisser seemed to think, may in part be the answer. For reasons, which the future perhaps will unfold, it has been more rapid within the past fifty years than for several centuries. So rapid has been the change that it has been noted in the experience of many men still living. Syphilis no longer expresses itself chiefly in gross cutaneous and osseous lesions, although such lesions are still frequent enough to require careful consideration in the study of the disease. It seems to have gone inward, as it were, and now spends its force on the internal organs—the great viscera and the cerebrospinal axis. From what I have just written, I do not wish the reader to infer that I incline toward the belief in special strains in the Treponema pallidum, such as a dermotrophic or neurotrophic strain. I emphatically do not. The attack of syphilis is determined solely by the *locus minoris resistentiæ*. The changes that have undoubtedly taken place in the onslaught of syphilis in civilized communities are due, I believe, to changes that have taken place in the individuals, which when studied in the mass go to make the general average of the disease as we now know it. To discuss them here would take us too far afield. At the present time by far the greater majority of syphilitics manifest the disease mainly as a serologic abnormality—a positive Wassermann reaction; yet, when we realize the vagaries and dangers of the infection, not one of these can be said to be safe from some unexpected catastrophe. Like Damocles they live with a sword hanging over their heads.

Whoever has a positive Wassermann reaction has syphilis.[1] This is an axiom that cannot be denied. In such a patient it may be impossible to discover clinically any other signs or symptoms of the disease, yet somewhere within that patient's body syphilis lurks, and who can say when it will not come forth to ravage and destroy. It has been asserted that to treat asymptomatic syphilis is like chasing a shadow—that those who do so are treating the Wassermann reaction but not the patient. This is not so. Behind that shadow is the important substance of a grave disease. For who can say that a positive Wassermann reaction in the blood or in the spinal fluid is not as much a symptom of syphilis as a gumma or a mucous patch. *Unless we have changed a positive Wassermann*

[1] For the few exceptions see the chapter on the Wassermann Reaction in Diseases Other than Syphilis.

reaction to a negative we have not cured syphilis. It must be admitted that this result cannot always be achieved. There are undoubtedly cases—usually those in which the infection has existed for many years, with or without symptoms—that no matter how much treatment or how skilfully administered, never change to a permanent negative Wassermann reaction. Such patients should be told that their syphilis is incurable. In these cases there undoubtedly continues to exist somewhere in the body a focus of the disease, although it may be impossible to locate it. Most frequently this focus is in the spleen, the liver, the cardiac musculature or the central nervous system. Patients with Wassermann-fast sera should, therefore, be carefully watched (even if asymptomatic) for any beginning involvement of these organs. These Wassermann-fast cases are not in the majority; they are much in the minority, but still a minority sufficiently large always to have to be reckoned with in rendering a prognosis as to the changing of a positive Wassermann reaction to a negative. The question of the percentage of changes from a positive Wassermann reaction to a negative I have discussed in detail in the chapter on Serology.

First Stage.—The patient who presents himself with a chancre, but whose blood still shows a negative Wassermann reaction, if treated intensively as outlined in the chapter on Treatment—that patient can be cured with almost mathematical certainty. By that I mean, that there will be effected not only a clinical cure of the primary lesion, which goes without saying, but a serologic and cytologic cure as well. His blood and spinal fluid will be normal and remain so.

The patient who presents himself with a chancre, but who has had that chancre long enough to cause the blood to become positive to the Wassermann test and the spinal fluid to react positively to the Wassermann test or to show other abnormalities as it does thus early in some cases—that patient can also be cured, but he will require more treatment than in the first instance. Such a patient should not be pronounced cured on the strength of a negative Wassermann reaction in the blood alone. A lumbar puncture should be done and the spinal fluid examined. If negative he can be discharged as cured; but if the fluid is pathologic, treatment must be continued intraspinally until it becomes normal.

Up to within a year after infection a cure can be promised in nearly every instance if intensive treatment is given. There are exceptions, however, but these are comparatively rare. These are usually due to individual idiosyncrasy and the *locus minoris resistentiæ* is most often found to be in the central nervous system.

Second Stage.—In late secondary syphilis, that is, within three years of the date of infection, the same results can be achieved,

but to a lesser degree. That is, in order to accomplish a cure more treatment must be given, and the failures to permanently change a positive Wassermann reaction to a negative will be greater.

Third Stage.—In the tertiary stage the same holds true; for while the lesions, as in the secondary stage, can almost invariably be made to disappear, except in some instances in which the nervous system is involved, in a general way it can be stated that the older the syphilis the more difficult it is to obtain a serologic cure. This applies not only to those cases in which there are active tertiary lesions but to those which are asymptomatic as well. But to tell such a patient that, no matter how old, his syphilis may be sterilized is wrong. It can often be done and until proven to the contrary, after a reasonable amount of treatment, the patient should be given the benefit of the opportunity. It is impossible to forecast in any given case whether a negative Wassermann reaction can be obtained or not.

The prognosis of acute syphilitic lesions in the secondary stage is invariably good with the exception of acute syphilitic nephritis. Some of these cases die or go on to chronic nephritis which cannot be said to be conducive to longevity. In the tertiary stage acute lesions *if promptly diagnosed and treated* can almost invariably be made to resolve. Exceptions to this are involvement of the motor oculi and auditory nerves, fulminant tabes dorsalis and acute myelitis. In subacute or chronic lesions, or rather the sequelæ thereof, especially of the viscera or nervous system, a sharp distinction must be made in the prognosis. The prognosis is here controlled to a great extent by the part involved and to a less extent by the length of time that the process has existed. All too frequently it is the sequelæ of these tertiary syphilitic processes which are treated under the misapprehension that since they are of syphilitic origin they can be influenced by antisyphilitic therapy, whereas they are the results of, rather than the actual process. For it must be remembered that tissue once destroyed cannot be restored. For example, gumma, or diffuse gummatous infiltration of the rectum, if treated while the cellular infiltrate is still in the proliferative stage can be made to disappear and leave no trace, but stricture of the rectum due to fibrous transformation of this infiltrate is absolutely uninfluenced by constitutional treatment. This applies without exception to every organ and tissue of the body.

Cutaneous gummata can almost without exception be cured. Those which remain seemingly uncured are almost invariably complicated with either tuberculosis or malignancy.

Bone Lesions.—Osseous lesions, with the exceptions to be noted, respond equally as well. Those which do not are complicated either

with tuberculosis, malignancy or pyogenic infection. If extensive caries has taken place so as to cause considerable destruction the osseous hiatus cannot always be filled in by proliferation of new bone. An example of this is to be seen in the saddle nose caused by the destruction of the osseous nasal bridge due to syphilitic disease. Exostoses and superimposed layers of proliferated bone that have become eburnated, such as occur on the forehead and the shins, cannot be made to disappear by treatment.

Eye Lesions.—Syphilitic lesions of the eye in the secondary and in the tertiary stages usually give a good prognosis. Synechiæ sometimes follow after iritis and in consequence thereof the pupil may be somewhat distorted. Prompt diagnosis and treatment, which includes keeping the pupil constantly dilated with atropine, usually prevents this however. Scotoma of any type, diplopia, anisocoria, miosis, loss of the reflexes to light or accommodation—each of these indicates involvement of the cerebrospinal axis, and the prognosis should be most guarded.

The Ear.—Syphilis of the auditory apparatus both in the secondary and tertiary stages—the last especially so—should always be given a conservative prognosis. Not infrequently these lesions are followed by complete restoration of the auditory function, but it is wise not to be too optimistic in promising this.

Gastro-intestinal Lesions.—The prognosis of gastro-intestinal syphilis, if promptly diagnosed and treated, offers a favorable prognosis. If fibrous changes have taken place, giving rise to stenosis or distortion—as "hour-glass stomach"—or stricture of the esophagus or rectum, the prognosis must be considered entirely from a surgical standpoint.

Nephritis.—As I have previously stated syphilitic nephritis, occurring in the secondary stage, should be given a guarded prognosis. Should uremia supervene a prognosis can be given if a lumbar puncture is done and the urea content of the spinal fluid is estimated. Canti found that in cases with a high urea content in the spinal fluid the outcome was invariably fatal, whereas those with a low content usually recovered. With the urea content below 0.3 per cent the prognosis is good; above 0.3 per cent recovery is extremely improbable.

Chronic interstitial nephritis occurring in the tertiary stage cannot be cured. The pathology of the condition will verify this. However, these patients may live for many years with their kidneys more or less crippled and may ultimately die of some intercurrent affection. Tertiary syphilis of the bladder, the prostate and seminal vesicles is frequently not diagnosed as such. If correctly diagnosed, however, these lesions usually respond promptly to treatment. The testicle is more frequently involved than any

other part of the genito-urinary tract in tertiary syphilis. Gummatous lesions, if treated in the infiltrative stage, respond promptly to treatment and the function of the organ is not impaired. Should sclerosis have developed and the testicle in consequence be reduced to a small fibrous nodule, the patient's sexual power will be impaired or completely lost according as whether one or both testes are involved. The flat plaques or plates of cartilaginous hardness, which sometimes insidiously develop in the corpora cavernosa, as a rule, do not respond to constitutional treatment. Their further progress, however, can be stayed, and it is sometimes possible to correct by surgical interference the deformity which may have arisen.

The Heart.—Cardiac syphilis is frequently not diagnosed. Unless there is a marked degree of myocarditis the prognosis is better than those cardiopathies arising from other causes. A peculiar fact to be noted in many of these cardiosyphilitics is that after apparent recovery they suddenly die. So constant is this occurrence that its possibility must be included in the prognosis. Arteriosclerosis due to syphilis offers a poor prognosis as to its chance of being influenced by antisyphilitic treatment. I have seen such cases benefited, but never cured.

The Lungs.—Syphilis of the lungs is rather rare and, therefore, is frequently unrecognized. Seemingly desperate cases have been known to go on to complete recovery when properly diagnosed and treated.

The Liver.—Gummatous disease of the liver, if not widespread or if promptly recognized, offers a good prognosis. If there has been much destruction of hepatic tissue or if the infiltration is extensive and advanced, the resolution of the process (as has been pointed out by Wile) leaves the patient worse than before, as the resultant scar tissue accentuates the cirrhosis and thus increases the tendency to ascites.

Ductless Glands and Anemia.—Syphilis of the ductless glands, and the anemias, which in some instances can be traced to syphilis, on the whole offer a more favorable prognosis than when arising from some other cause. The same is true of amyloid disease which is distinctly more favorable when caused by syphilis than when due to tuberculosis or prolonged suppuration.

Nervous System.—Syphilis frequently attacks the nervous system both in secondary and tertiary stages of the disease. Occurring in the secondary stage, syphilis of the nervous system of any form offers a good prognosis if treated promptly and vigorously. This does not include freedom from later attacks, as these early nervous lesions connote a susceptibility of the nervous system which should always be a matter of concern. These cases should be kept under

observation for a period of years—at least five, and the blood and spinal fluid examined at regular intervals. After that time if the blood and spinal fluid have remained normal a favorable prognosis as to the nervous system remaining free from future involvement may be given.

In tertiary syphilis of the nervous system the prognosis depends largely, in my opinion upon the time when the diagnosis is made. Lesions that are correctly diagnosed as soon as they occur and are vigorously treated, in a surprisingly large number of instances can be cured. It is the neglected or incorrectly diagnosed cases that fail to respond to treatment. Especially is this true of the two most formidable manifestations of tertiary syphilis of the central nervous system—tabes and paresis. I desire to go on record as deploring the attitude generally assumed by most physicians when confronted with these two forms of nervous syphilis. If diagnosed early and treated intensively both are possible of cure or at least their progress may be checked and the patient given a respite that may last through life, or for many years. However, in these cases the same strict watch over the blood and spinal fluid must be held as already mentioned as necessary in secondary nervous syphilis. In these instances it is perhaps, if anything, more necessary, as the danger of relapse is correspondingly greater.

Congenital Syphilis.—The prognosis of congenital syphilis as to life or the persistence of dystrophies should in a large number of instances be guarded. Congenital syphilis takes a larger toll of infant lives than any other disease. If the lesions are mild or do not involve the viscera a favorable prognosis can nearly always be given. If the lesions are severe and marasmus is marked, guarded prognosis must be given. Many of these infants die in their sleep or die suddenly from no seemingly ascertainable cause. Cases in which the cutaneous lesions become pustular usually terminate fatally.

There is no disease for which we possess such certain means of cure as syphilis. At our command are instruments which can be made to act with the same precision as those of the surgeon. As with the surgeon, knowledge and skill in their use and the ability to decide when to apply them will produce results many times equalling and even surpassing the most brilliant efforts of the boldest and most skillful wielder of the knife, the clamp and the forceps.

CHAPTER XVI.

THE TREATMENT OF SYPHILIS.

Specifics.—In the treatment of syphilis there are three drugs which are specific; that is, they almost without exception produce a certain desired effect upon the processes of the disease. These drugs, in the order of their importance, are organic arsenic, mercury and potassium iodide. Either of the first two, if used alone, will cure the disease; for reasons, which will be detailed later, they are both used in the treatment of the disease. Potassium iodide, the last of this therapeutic triad, will of itself not cure syphilis, and its administration has no effect whatsoever upon the organism of syphilis—the Treponema pallidum. Its action is to cause an absorption, or rather an elimination, of the morbid products of the disease. It also assists in the elimination of the mercury which, when this drug is used in certain forms, becomes stored up in the body, mostly in the liver, and thus assists in the latter's curative effect because mercury only exerts this effect while it is in a state of flux or when it is being eliminated from the body. Thus it will be seen that potassium iodide is an adjuvant to mercury and intensifies its action as well as causing the morbid products of the disease to melt away. For this reason, in the tertiary stage when there are new formations caused by the disease it is given in combination or in conjunction with mercury.

Arsenic.—The foremost—the most powerful—of these specifics for syphilis is organic arsenic—known under various names, such as arsphenamine, salvarsan or "606." This latter name was given because it was the six hundred and sixth preparation that Paul Ehrlich, its inventor, had tried, and he thought that it represented the "therapia sterilizans magna"—the great sterilizing medicine in the cure of syphilis. Ehrlich did not succeed in producing a remedy that at once would neutralize the treponemata, but he at last succeeded in making the greatest therapeutic advance that has yet been made in the treatment of the disease and, with the technic now in use, has almost succeeded in producing the sterilizing effect he sought.

It was the discovery of the Treponema pallidum by Schaudinn and Hoffmann, in 1905, that gave a new impetus to luetic therapy, because it brought to light chemical and biologic possibilities

hitherto unknown. Arsphenamine was no haphazard or accidental discovery. It is the logical result of a long series of investigations and experiments carefully planned with a definite end in view. It represents the culmination in an evolution of therapeutic experiment. It is a true child of science; empiricism has nothing to do with it.

Arsenic is eliminated mostly through the kidneys, and this elimination is practically accomplished within twelve hours—the amount remaining in the tissues thereafter is so slight as to be negligible. Reasoning from this von Notthaff and also Scholtz in Germany, gave the drug at much shorter intervals than usual, their idea being to keep the tissues continually bathed as it were in the treponemacidal fluid, thus accomplishing the sterilization anticipated by Ehrlich. With this object in view they gave the drug at intervals of twenty-four hours for three doses. The results they achieved were so satisfactory that they advocated this treatment as superior to that of giving the drug at wider intervals. Owing to the War this method remained unknown in the United States until it was introduced by Pollitzer. This "intensive method" is applicable to any phase of syphilis and with certain exceptions it is the method that I invariably follow. These exceptions are in congenital syphilis of infants and young children, in the aged and in tabetics who are markedly debilitated. As Kolmer, Broadwell and Matsunami have shown, the antibodies generated by the disease are strongest in the latent tertiary stage, that is when the only evidence of syphilis is a positive Wassermann reaction. Many of these patients are "Wassermann fast" and no amount of treatment can change the serum reaction. The object of treatment in these cases is to maintain the formation of antibodies at as high a level as possible and thus hold the disease in check. For, as stated by Eberson, "A state of latency would imply a balance that has been struck between the antibodies and the invading spirochetes." To destroy this balance by giving an overdose of arsphenamine as it were, which would depress the power of the tissues to form these antibodies, would be unwise. Unless to attack some definite lesion, intensive treatment is not called for in these cases. The purpose of treatment should be to maintain or even to augment this antibody formation; and this can be best accomplished by giving the drug at wider intervals.

Arsphenamine.—Arsphenamine contains 31.57 per cent of arsenic. It is a standardized product under the supervision of the United States Government. Its chemical name is dioxydiamidoarsenobenzol. It comes as a yellow powder, easily oxidized and hygroscopic and for that reason is dispensed in hermetically sealed tubes or ampoules containing an indifferent gas, such as nitrogen, to

prevent chemical change. Because of this, it is absolutely necessary from its readiness to decompose and form highly toxic compounds, that the contents of the ampoule should be prepared as soon as opened, and the prepared solution should not be kept longer than a half hour after it has been made. Personally, I do not allow it to stand even that long but inject it immediately after it is prepared. This is the safe plan to pursue.

Neoarsphenamine.—Because of the difficulties sometimes encountered, and also to lessen the bulk of the solution, Ehrlich later introduced neoarsphenamine, the preparation of which is more simple. It is the consensus of opinion, however, among clinicians who have used it, that the newer drug is much less potent in its effect than the arsphenamine. This is undoubtedly due to the less amount of arsenic which it contains. Therapeutically it is about three to five, *i. e.*, three old arsphenamines are equivalent to the action of five new arsphenamines. Personally I prefer neoarsphenamine to arsphenamine. While neoarsphenamine is undoubtedly less active therapeutically because its arsenic content is less this can be very easily overcome by simply increasing the dose. By thus increasing the dose the therapeutic activity of the newer drug can be automatically raised to the level of the older drug. Neoarsphenamine has also the advantage of not requiring such a high dilution as arsphenamine. A dose of 0.9 gm.—the usual dose of neoarsphenamine for an adult and practically equal to 0.6 gm. of arsphenamine can be given in from twenty to thirty cc of water. This is the dilution of Thibierge and the one which I am in the habit of giving. Since a powerful dose can be given in such a small amount of water the danger of throwing a large amount of fluid suddenly into the circulation is obviated, which is a very important consideration in certain cardiac conditions such as chronic myocarditis or aneurysm. While it is not generally known perhaps, my personal experience is that the introduction of arsphenamine is quickly followed by a lowering of the blood-pressure.

Kolmer, Schamberg, Raiziss and Weiss have shown that solutions of arsphenamine have an undoubted hemolytic power. They ascribe this hemolytic activity to three factors: (1) The direct hemolytic activity of arsphenamine; (2) the hemolytic activity of non-isotonic solvents—plain water or a hypotonic saline solution; (3) the hemolytic activity of sodium hydroxide used to neutralize the solution. Further, which is important from the clinical standpoint, they reported neoarsphenamine to be devoid of these hemolytic properties. This I may add is another advantage which the newer drug has over the older. Kolmer and Yagle also showed that concentrated solutions of arsphenamine are more hemolytic than dilute solutions. The use of sterile, *fresh* distilled water

seems to possess advantages over sterile, stale distilled water as regards toxicity, although the difference noted in their experiments was not pronounced. Arsphenamine in alkaline solution quickly undergoes oxidization on standing with consequent increased toxicity. If two or three hours delay are unavoidable in using the drug, the solution should be kept in a glass cylinder *full to the stopper* so as to absolutely exclude the air.

Schamberg has also recently shown that unduly agitating the solution either of arsphenamine or neoarsphenamine greatly increases the toxicity of these drugs. Excessive shaking or the formation of air bubbles by forcibly expelling the solution that has been drawn up into the syringe should not be done as dangerous oxidization products are thereby formed.

Schamberg, Kolmer and Raiziss also called attention to the fact that arsphenamine and its congeners are not compounds of absolute purity and, therefore, absolute constancy in biologic effect cannot be obtained. This being so, arsphenamine and its congeners may and do vary within certain limits in therapeutic effect, and to a greater degree in toxicity. This variation in toxicity is noted to a striking degree in ampoules purchased in the open market. The investigators believe that the drug should be tested both intravenously and subcutaneously to the extent that it should be tolerated by rabbits in the dose of 60 mg. per kilo of body weight. They further maintain, as a result of their experiments, that arsphenamine is, on the whole, a safer drug than mercury. They proved this by the fact that it can be tolerated intravenously in white rats at fifty times the dose of mercury, weight for weight.

Kolmer and Schamberg demonstrated on lower animals and later on man that arsphenamine can be given in pills, capsules and in solution, without producing any untoward symptoms, and, in the case of man, with some slight therapeutic effect. This therapeutic effect in man, however, is so much less than when it is given intravenously, that I shall not discuss it further as I do not consider it worth while.

Intravenous Administration.—Arsphenamine or any of its congeners should only be given by the intravenous route. It is the only way whereby its most potent therapeutic effect can be obtained. Of late there have been some who have advocated giving arsphenamine by the rectum. I have tried it but have discontinued it, as I am convinced that the therapeutic effect produced is so insignificant that its further use is unwarranted. I mention the intramuscular and hypodermic methods only to condemn them. Nor do I consider of any practical use arsphenamine pastes for syphilitic skin diseases which have been advocated by some. I do not believe in giving it in very small doses except where some

of the cranial nerves are involved. In the last instance I consider it a far better plan to precede the arsphenamine, *i. e.*, to control the nerve lesion first by intravenous injections of mercury, rather than to use a smaller dose of arsphenamine. Arsphenamine should be given on an empty stomach and the bowels emptied previously by a mild aperient, such as a solution of citrate of magnesia.

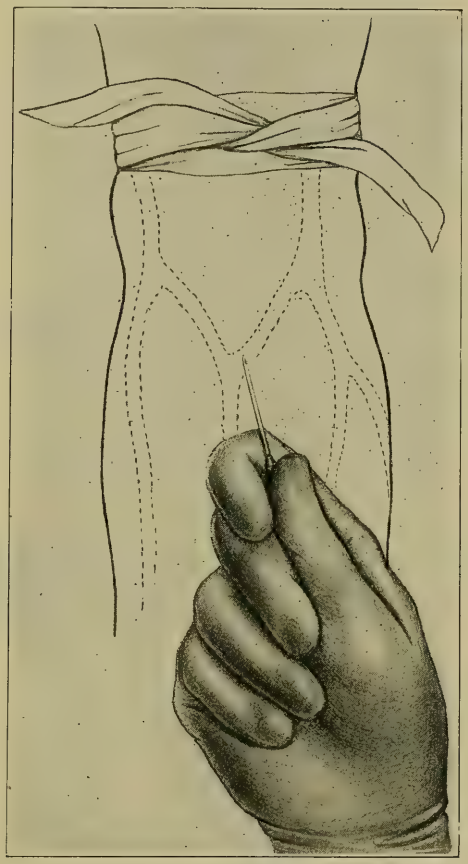


FIG. 50.—Wrong way of holding needle.

Food should not be eaten for at least four hours after arsphenamine has been given. In very many cases following the administration of arsphenamine there is a slight reaction manifested by vomiting, diarrhea, chills and general malaise. This may be due to using stale water, as the Yakimoffs have proven that the endotoxins contained therein will produce this. While this is undoubtedly

true, the same symptoms are frequently seen when the water used is absolutely freshly distilled. In my opinion when this reaction

FIG. 51.—Veins at bend of elbow.

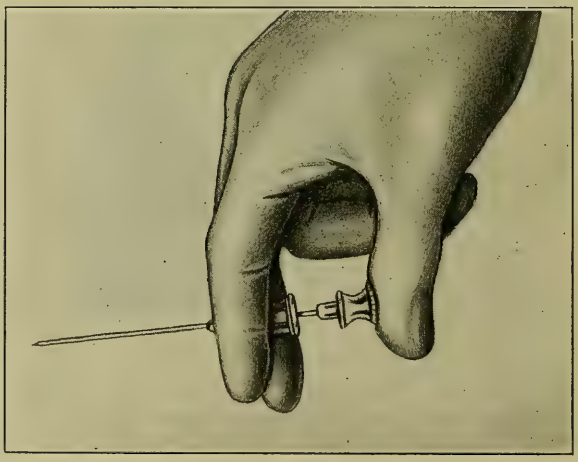


FIG. 52.—Correct way of holding needle.

occurs it is of an anaphylactic nature. Arsenic can be detected in the blood simultaneously with the injection and in the urine

voided immediately after the drug has been introduced into the body. Excretion is mostly through the kidneys and, to a less extent, through the intestinal canal. Transient albuminuria is sometimes observed after the administration of the drug, but it does not injuriously affect healthy kidneys, and from an extensive

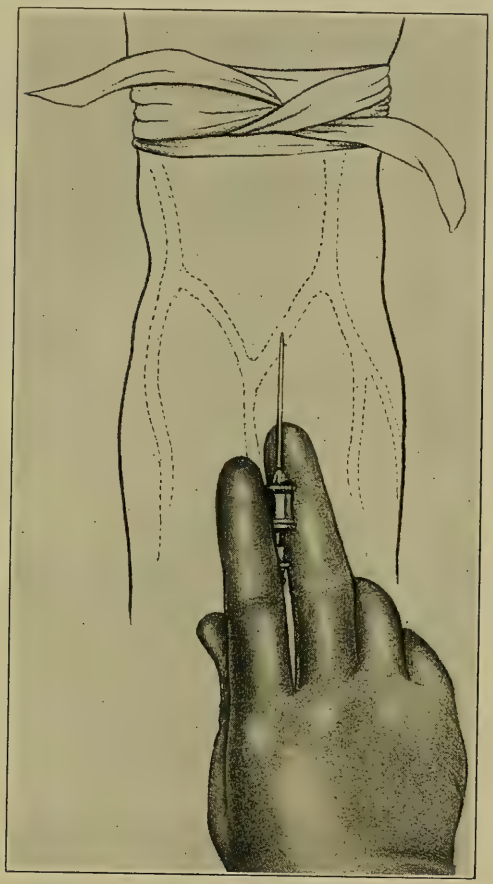


FIG. 53.—Correct way of holding needle.

experience I do not believe that it is as dangerous as some claim, to kidneys that are diseased. After the reaction that usually follows the administration of arsphenamine, the patient usually experiences a feeling of stimulation and well being, which according to Schreiber and Hoppe is due to the stimulating effect of the arsenic on the lecithin metabolism.

Jarisch-Herxheimer Reaction.—A phenomenon frequently observed after the injection of arsphenamine and also, although much

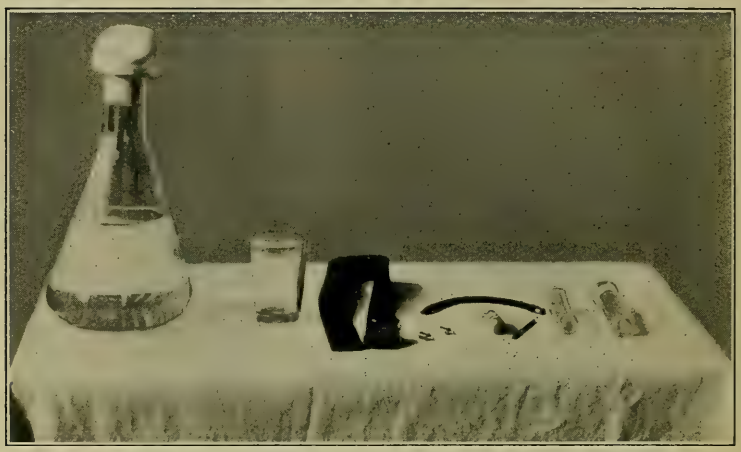


FIG. 54.—Apparatus for intravenous injection of arsphenamine.

less frequently, after the injection of mercury, is the so-called *Jarisch-Herxheimer* reaction. This is an inflammatory reaction produced in syphilitic lesions due to the action of the specific treatment. The occurrence of this reaction, which I may say is not in-

FIG. 55.—Syringe and arsphenamine solution.

variably present when arsphenamine is given, has been variously explained by different observers as due to a liberation of syphilitic

endotoxins causing a hyperemia; excitation of the Treponema pallidum to increased activity by insufficiency of the dose; individual irregularities in the vascular tonus. While there is undoubtedly truth in all of these explanations, the probabilities are that it is a purely anaphylactic reaction. The symptomatology of the reaction is quite varied. On the cutaneous surface the eruption, if present, is made more intense or, if it is not present, edema and a generalized redness of the skin may occur. Mucous patches, if present, react in a similar manner. Gummata may become swollen and ulcerate before improvement is shown. In cerebral gummata these facts of exacerbation should be known and borne in mind when arsphena-

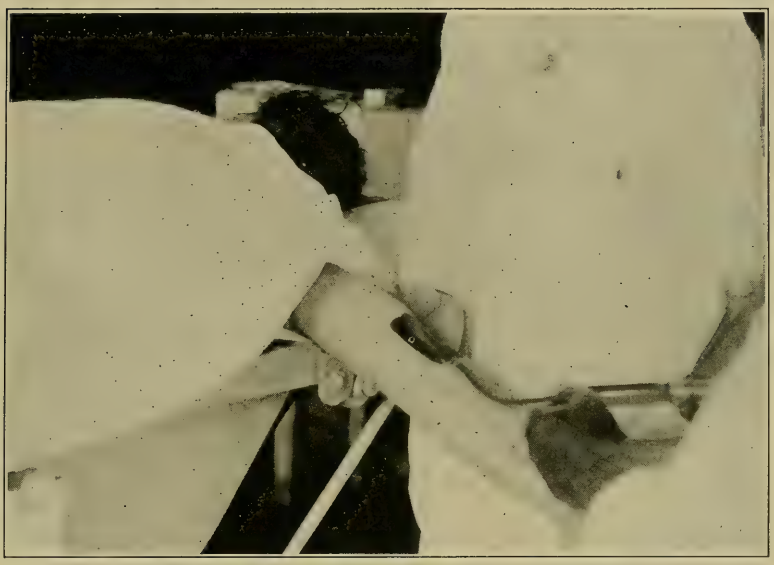


FIG. 56.—Giving intravenous injection of arsphenamine.

mine is to be given. Gummata of the other viscera react in a similar manner. There may even be fever, jaundice and albuminuria, and these symptoms may last for a week or longer when they gradually decline or they may go on to a fatal termination; this last I will discuss later. It is the nervous system, however, which is most profoundly affected by the reaction. Especially is this true where the cranial nerves pass through rigid, bony canals, which allow compression of these nerves by the inflammatory exudate. In cerebral lues the reaction usually manifests itself as a severe cephalalgia, but where focal lesions exist the exudative character of the reaction may cause irritative and paralytic symp-

toms of a grave character. The severe pains following arsphenamine treatment in tabes are of this character.

Contraindications.—Arsphenamine is not altogether devoid of danger. In certain conditions it is absolutely contraindicated or, if given, it should be given with extreme caution. It is contraindicated in severe bronchitis or in bronchiectasis. In iritis it should be preceded by mercury. In cardiac lesions it should be given with caution, at least if the condition is due to lues it should be preceded by mercury and, when administered, given in a more concentrated form than is usual. At least a month should be allowed to elapse between treatment with these two drugs. Treatment with mercury before arsphenamine predisposes to liver injury by arsphenamine and to nephritis and also to encephalitis hæmorrhagica. In regard to the administration of arsphenamine after a course of mercury, an intervening period should be allowed. Arsphenamine should *not immediately* follow a course of mercury. If the patient has been taking some inorganic form of arsenic, such as Fowler's solution or arsenous acid, arsphenamine should not be given until several weeks at least have elapsed after the discontinuing of these drugs. If the patient shows a marked idiosyncrasy to arsphenamine, as evidenced by skin eruptions following the use of the drug, a wide interval should be allowed to elapse before giving it again.

Nitritoid Crisis.—The term "nitritoid crisis" which was applied to this phenomenon by Milian is incorrect. While the symptoms undoubtedly resemble those caused by acute nitrite poisoning very closely their kinetics are different. "Nirtitoid crisis" is therefore an improper term for these symptoms. Girbal would make a distinction between anaphylactic or colloidoclasic shock and nitritoid crisis following the intravenous injection of arsphenamine but in the light of present knowledge this distinction is hardly tenable. The anaphylactic reaction just described in some instances may come on suddenly, either during or immediately following the administration of arsphenamine. It may be that the injection is proceeding satisfactorily, when suddenly it is noticed that the patient is becoming cyanotic, or it may be that instead of the cyanosis a decided redness of the face occurs. The lips swell and become bluish and the swollen tongue protrudes. The conjunctiva is injected and there are symptoms of air hunger. The patient breathes stertorously. The patient lapses into unconsciousness and there is involuntary evacuation of the bowels and the bladder. Altogether the picture is most alarming. The face is covered with sweat and the pulse is weak and thready. These attacks are rarely fatal, although fatalities have been recorded. Slowly the patient regains consciousness, the color becomes better

and the air hunger disappears. The patient feels dazed and weak and desires to go to bed. In a certain number of patients, almost invariably after the first injection—the second or third, or even fourth or fifth—an acute reaction occurs which partakes of the nature of an anaphylactic shock. The subject of arsphenamine anaphylaxis has been extensively investigated within the last two years, and has brought to light many new facts which have very materially changed our former conceptions of this phenomenon especially as it is caused by organic arsenic. We now know, thanks to the work of Kopaczewski, Lumière, Gautrelet, Chevrotier, Widal, and others that this reaction is physical rather than chemical and is due to an upset in the colloidal equilibrium in the body. The shock which arsphenamine caused is humoral in type and its clinical and histologic manifestations are the result of a sudden flocculation or lysis in the blood of its formed elements. Primarily it is due to the patient's idiosyncrasy to arsenic and is therefore inherent and is in no way caused by some impurity in the drug, although it cannot be denied that impurities can be formed that will produce untoward symptoms either as the result of faulty manufacture or improper immediate preparation. Because of this rupture of the physical equilibrium of the colloids of the organism of which the symptoms about to be described are the expression, Widal and his associates have designated this particular form of anaphylaxis by a more definitely descriptive term—"colloidoclasis."

Much research has been done to devise a means whereby this shock can be prevented. After experimenting with many reagents, Lumière and Chevrotier found that sodium sulphocyanide, sodium ethylsulphate and sodium hyposulphite would prevent the reaction from occurring when injected intravenously five minutes before the arsphenamine is to be injected. Sixty cc of a 5 per cent solution of any one of these substances can be used. Sicard and his coworkers found that the preliminary injection of 60 cc of a 2 per cent solution of sodium bicarbonate is equally efficacious. In addition to this procedure, in order to limit or localize the reaction should it occur, to the part in which the injection is made, a constricting band or tourniquet is applied above the point of injection which in most instances is in one of the veins of the forearm. If hemoclasis occurs it is restricted to the locality below the constriction which is removed five or six minutes later. Sicard calls this procedure "arsenical anticlasis by topophylaxis."

A rarer form of reaction to the drug is the so-called serous apoplexy, or perhaps a better term would be hemorrhagic encephalitis. It is sometimes preceded by the nitritoid crisis, but in a somewhat extensive experience I have never observed this. It usually does not occur until two or three days following the injection of the

drug, during which time the patient may not complain. The patient then complains of malaise, of headache and frequently vomiting occurs. He soon becomes so ill that he takes to his bed and usually, shortly after, either becomes comatose or is attacked with epileptiform seizures, either tonic or clonic, or a combination of both, after which the patient goes into a gradually deepening coma with the respirations becoming shallower and shallower until death closes the scene, the whole time of the illness being not more than twenty-four to forty-eight hours.

Milian is of the opinion that the condition is due to adrenal insufficiency augmented by the vasodilator effect of the arsphenamine. Autopsy shows cerebral edema and separation of the nerve fibers and numerous punctate hemorrhages throughout the brain. In a series of eight cases autopsied by Warthin there was degeneration of the renal cells, which accounts for the suppression of urine observed in some of these cases.

Jaundice.—A second rare danger of arsphenamine administration is the development of a fatal jaundice following shortly after the drug has been given. The observations of Bailey and Mackay on syphilitic patients undergoing treatment with organic arsenic, show they are in a large measure protected from liver damage by a diet rich in carbohydrates and low in fat and protein. Such diet should precede and follow the treatment by arsphenamine. especially if the intensive method is used for several days. The reasons for it are based upon facts that cannot be controverted Davis and Whipple in their studies of liver damage and repair in dogs poisoned by chloroform, noted that sugar and diets rich in carbohydrates, fed to the animals for several days preceding the chloroform narcosis, exercised a marked protective action against injury to the liver. Fats alone, or in combination with other food increased the susceptibility to liver injury. A diet of skim milk and bread or cereal, or any other diet of carbohydrates exclusively exerted the maximum defense to the liver cells. The importance of such a protective diet can be readily appreciated, especially when giving such a drug as arsphenamine which has a selective deleterious action on the hepatic cells. Jaundice as a concomitant of secondary syphilis, while rare, occurs with sufficient frequency to have caused it to be noted by all syphilologists It is due to a duodenal catarrh or to a catarrh of the small bile ducts or probably of both. It is quite possible, therefore, that in these cases where severe or fatal jaundice develops after the administration of arsphenamine, there has been already some damage to the liver cells. (The jaundice is due to retention caused by damage of the hepatic cells by the Treponema pallidum.) As is well known, arsenic acts also on the liver cells and this effect com-

bined with the previous effect caused by the organisms of the specific disease is sufficient to cause the icterus. In other words, given a syphilitic hepatitis and then further insult the damaged organ with arsenic, a drug which can cause the degeneration of the liver cells, and jaundice will ensue. The condition is ushered in with nausea and vomiting, and may occur from twenty-four hours to three weeks subsequent to the administration of the arsphenamine. The icteroid symptoms do not differ from those due to other causes. The jaundice may be only slight or it may be deep. There is itching of the skin, clay colored stools, bile in the urine, albuminuria and bradycardia. The symptoms usually clear up in one or two months, but in some instances death may result.

These conditions are rare, but it must always be remembered that they may be unexpectedly met with, and that by some one who may not be experienced in combating these conditions.

Colloidoclasic shock cannot be presaged, although it is more apt to occur in that class of individuals usually designated as "flabby," that is, those pale or pasty complexioned and rather stout persons who are good livers and who are not inclined to exercise any more than is abolutely necessary It is possible that the use or abuse of alcohol may be a factor in these cases.

In the treatment of the so-called serous apoplexy or hemorrhagic encephalitis, adrenalin should also be given. In these cases it is permissible to give it intravenously; that is, 1 cc of adrenalin in 100 cc of normal salt solution. This should be repeated in three or four hours. In the meantime, high irrigations of hot-salt solution should be given with poultices of hot digitalis leaves in flaxseed meal over the loins. Cupping over the loins may also be tried. Venesection and saline infusion and lumbar puncture should also be employed. The adrenalin should not be given by the mouth, as it is sometimes vomited immediately. If there is evidence of acidosis, intravenous injections of a 2 per cent sodium bicarbonate solution should be given.

The jaundice caused by the administration of arsphenamine is difficult to forefend. Should the patient show, upon examination, tenderness over the hepatic region, or if there is enlargement of the liver, or if syphilitic jaundice already exists, arsphenamine should not be administered, but the patient should be placed under mercury and potassium iodide until the condition clears up, and even then several weeks or a month should be allowed to elapse before arsphenamine is given. Scott and Pearson state that these patients, while the drug is being administered, complain of tasting and smelling it. I cannot say that I have ever observed this. The patient should be put to bed and free catharsis instituted. A milk diet should be

given, and once or twice a day the patient should receive a high rectal enema of *cold* normal salt solution. Two to 3 liters of water should be used. Iodide of potassium in doses of 20 minims of the 100 per cent solution should be given t. i. d. in a glass of milk. The patient should also receive an injection into the buttock of 3 cc of intramine, which should be repeated in three days, and then at the end of six days another injection of 5 cc should be given. The patient should not receive mercurial treatment until the icterus has entirely disappeared and then it should be exhibited with caution. Arsphenamine should not be administered for at least six months, or until all possibility of the toxic action of the drug is removed.

Intravenous Administration.—For the intravenous injection of arsphenamine there are many different forms of apparatus. They are all good, although many, in my opinion, are needlessly complicated. Personally I prefer a large glass Luer syringe, holding not less than 30 cc and a straight gold needle—the gold needle because it does not corrode and thus clog the lumen. To this is attached a rubber tubing of about the caliber of a No. 12 French catheter. The vein most frequently used as the site of the injection is the median cephalic, which in most instances can be found on the anterior surface of the arm at the bend of the elbow, although any vein that is sufficiently prominent will do. The patient should be in the recumbent position and when the tourniquet is applied, which may be a rubber band or a catheter held tight by an artery clamp, or even an ordinary roller bandage, he should be instructed to clench his fist, which causes the veins of the forearm to stand out more prominently. A smart slap over the veins will also cause them to appear to better advantage. The needle should be introduced at a slight angle to the vein and directly into it. Some insert the needle to the side of the vein and then enter when beneath the skin. This technic is, I might say, largely a matter of training and practice. Where the veins are deeply seated they can often be felt by the practiced tactile sense. Care must be taken not to infiltrate the surrounding tissues as a painful abscess will result if this is allowed to occur. Should this accident happen, as it will occasionally even with those who are skilled, the needle should be immediately withdrawn and another insertion made. The infiltrated area should be well massaged to spread the solution and thus avoid its being concentrated in one area, and a tight bandage applied and the patient instructed to make hot applications to the part later. It is to be understood that while injecting, no air should enter the vein, although in my opinion, the danger of air bubbles in the administration of arsphenamine is very much overestimated. It is needless to state that the most careful asepsis should be preserved throughout the operation. The amount of

arsphenamine should be 1 dcg. for every 25 pounds of body weight in man, and 1 dcg. to every 30 pounds of body weight to a woman. The solution should not be made until the water, which must always be distilled, is cold. Do not, under any circumstances, inject or prepare the solution with *hot* water. For every decigram of arsphenamine in solution 4 drops of a 15 per cent sodium hydroxide solution should be used to neutralize it. The proper method of preparation of arsphenamine, or any of its congeners, is told in the wrapper which invariably accompanies the ampoule, and for that reason I shall not go into these details.

Silver Salvarsan.—Within the last few years a new form of arsphenamine has been introduced in Germany, and is now coming into use in the United States. This is silver salvarsan, for which a superior therapeutic effect is claimed. It is also said to be less toxic than the older form of arsphenamine. According to Kolle, it contains 22.4 per cent of arsenic and 14.1 per cent of silver. The silver is not present in the oxide or colloidal form, but as a complex combination between a colloid and a crystalloid. According to Bauer the relative chemotherapeutic coefficient is silver salvarsan 1 to 25, as compared to 1 to 10 to neoarsphenamine. The dose of silver salvarsan is from 0.1 gm. to 0.3 gm. dissolved in from 30 to 90 cc of doubly distilled water. It is advised to inject the solution very slowly. Some of the German users of the drug advise against the use of mercury in conjunction with it. I am not in accord with this. I believe that mercury should never be omitted in the treatment of syphilis.

The consensus of opinion among those who have used silver salvarsan extensively is that it marks an advance over the older forms of arsphenamine. It is possible that this is true but I believe the dose should be larger than is now recommended to be used. Unless this can be done without the possibility of argyria I still prefer the older form of the drug. As it is now, I believe silver salvarsan can be used with advantage in children, the aged, in cardiopathics and in some instances in syphilis of the nervous system. As time goes on its advantages and disadvantages will be more clearly recognized, and if it is destined to replace the older forms of organic arsenic because of its superiority it will do so; otherwise it will not.

A form of arsphenamine known as sodium arsphenamine has been in use in Germany since 1915. It is only recently that it has been used in this country. It is said to possess the therapeutic qualities of old arsphenamine with the added advantage of being soluble in plain distilled water in low dilution—20 cc. Its therapeutic qualities do not seem to be any greater than its congeners old or new arsphenamine. Since old arsphenamine is more active

therapeutically than neoarsphenamine and sodium arsphenamine is said to be equal to it therapeutically, it follows that it can be advantageously used in its place since it is prepared in the same manner as neoarsphenamine. I have not used it but those who have in Germany and the United States—Wright and Michelson and Siperstein—report upon it favorably in so far as its therapeutic action equals but does not excel the older forms of the drug.

Mercury.—The second drug in the therapeutic triad of syphilis is mercury. Since the days of Paracelsus, and in my opinion long before, it has been our most potent weapon of attack on syphilis. Now it has been overshadowed by arsphenamine, but its usefulness is by no means a thing of the past. Without its powerful help I do not think we could cure syphilis even with arsphenamine. There is a tendency at present to treat syphilis without mercury. This I hold to be a mistake. Mercury is still necessary in the treatment of syphilis. It is the army of reserve after the attack by arsphenamine. If arsphenamine can slay its tens of thousands of treponemata, mercury can at least slay its thousands. While it may not act as rapidly as arsphenamine yet it acts as surely. If arsphenamine alone can cure syphilis, so can mercury. Therefore, it should not be cast aside; because it plays a part in the treatment of syphilis that is indispensable. Its part is to reinforce the action of arsphenamine; it follows after and continues, as it were, the battle begun by arsphenamine until the foe is utterly annihilated. Mercury, like quinine for malaria and opium for pain, is a true specific. For that reason, if no other, its potent power should always be employed in the treatment of the one disease which, more than any other, will not respond but to a specific drug.

The metal mercury itself is inert, but when it combines with the fluids of the body it becomes active. Mercury passes out of the system by way of the urine, stools and saliva, as a sulphide. It is while mercury is being excreted that its therapeutic action becomes apparent. It is excreted slowly and, therefore, it tends to accumulate in the body. The residue that is not excreted causes the symptoms that we know collectively as mercurialism or ptyalism. It is a well-known fact that mercury has the power of "relieving tissues encumbered with superfluous and obstructive material." It is this cumbering of the tissues that is precisely what exists in syphilis, and mercury should, therefore, be administered not only as an antidote to the Treponema pallidum, but also to remove these morbid products as fast as they are formed, until finally the impression upon the bodily organism has been made to disappear. Every method of treatment since the days of John of Vigo—with the exception of arsphenamine—has had this object in view—the recovery to normal of morbid tissue changes and the rapid elimination of the morbid products.

Although mercury, next to arsphenamine, is the most powerful antisyphilic remedy known, yet strange to say it is not a spirocheticide. Recently, Schamberg and others have been experimenting with the various forms of organic mercury, but as this is written they have nothing definite to offer. The field is a fertile one, however, and the possibilities are great.

Administration of Mercury.—There are many ways of administering mercury, some of which are impractical and, therefore, rarely used. Mercury may be given by mouth, by inunction, by intramuscular injection, by intravenous injection, by suppositories, by fumigation, and by baths. Of those, intravenous injection and inunction are by far the best. Intramuscular injections of an insoluble salt were first used by Scarenzio, of Pavia, in 1864. Owing to the constant formation of abscesses because of lack of aseptic technic—this was before Lister's great discovery—the method quickly fell into disuse and we hear no more about it until it was again brought forward by Smirnoff in 1882. He showed that with antiseptic precautions—this was before the days of asepsis—injections could be given without the occurrence of abscesses, that is, they did not occur as often as before. They were frequent enough, however; so much so, that the method again fell into disuse. It was taken up again by Balzer in 1888, who pointed out that the chief causes of abscess formation were: (1) That the injections were given into the subcutaneous tissues instead of into the deep tissues, and (2) because of the vehicles to suspend the mercury. Balzer advocated deep injections into the muscle and the substitution of liquid paraffine as a vehicle instead of acacia, glycerin or olive oil as had formerly been used. His suggestions were followed by the best results, and from that time on the intramuscular method has grown in popularity until now its use is almost universal. The advantages of the intramuscular method are obvious; it is convenient both to the patient and to the physician; it insures regularity of treatment, and it leaves the stomach free; it insures accuracy of dosage, and the absorption of the medicament is much more certain, and consequently its therapeutic effect. The disadvantages of the intramuscular method are pain at the site of the injection. This pain, however, in my opinion, is comparatively relative and depends largely upon the idiosyncrasy of the patient. Some do not complain at all, while others refuse the treatment because of the pain. Some years ago Lambkin devised a mercurial cream which was supposed to be used without causing any pain. In my hands, however, it did not come up to expectations. Another disadvantage in the use of intramuscular injections is the suddenness with which the patient sometimes becomes salivated, and when salivation occurs when intramuscular injections has been

given it is most refractory. This salivation is due to the sudden release of injections that have become encapsulated and the consequent sudden flooding of the system, as it were, with the drug. Intramuscular injections should not be given to women unless the needle is long enough to completely penetrate the panniculus adiposus of the buttocks, as when mercury is injected in fatty tissue it is not absorbed but almost invariably causes abscesses to form.

Suppositories.—A convenient and efficacious manner whereby mercury may be given is by suppositories. They were recommended by Bryant in 1884, but more than seventy years before they were used by Larrey, the surgeon-general of Napoleon's armies. They can be prepared either with gray oil or with blue ointment; to this should be added a small amount of cerate and also 0.015 gm. of extract of hyoscyamus. A suppository may be inserted every night for a month. While this method is not the ideal, yet it is in my opinion superior to oral medication.

Fumigation.—Fumigation is one of the oldest methods of mercurial administration. It was much in vogue in the sixteenth century when it was combined with sweating and large doses of guaiac.

> "Wonderful little, when all is said,
> Wonderful little our fathers knew.
> Half their remedies cured you dead—
> Most of their teaching was quite untrue."
>
> *Kipling.*

To give a mercurial fumigation the procedure is as follows: The patient sits naked on a wooden cane-seated chair or commode, and is covered in a cloak-like fashion with a blanket, the head being free. Thirty grains of calomel are vaporized over a spirit lamp under the chair, care being taken that the vapor is not inhaled. The volatilization of the calomel takes about fifteen or twenty minutes, but the patient should remain seated and covered for fifteen minutes longer. The patient is then put to bed for an hour. Fumigations may be given every day, or less frequently, according to circumstances. They may be continued for a month or longer. This form of treatment is of benefit in obstinate skin lesions, chiefly on account of its local effect. As a routine treatment it is of little value, and since the advent of arsphenamine is now rarely used.

Baths.—Mercurial baths are sometimes used, especially for infants with inherited syphilis. They have no special advantages and as there are other and better methods for treating congenital lues I shall do no more than mention them.

By Mouth.—The oral administration of mercury by pills and solutions is, of course, still used, as it has always been. It is now rightly falling into disuse. I desire to go on record as condemning

it absolutely as a routine method of treatment. I have never known it to render a positive Wassermann negative. If used at all it is at best but a makeshift for other and better methods. If, however, for some reason it is impossible to give any other treatment, the best form to give it in is mercury and chalk combined with Dover's powder, equal parts, beginning with 1 grain and going up to 10 and continuing until the gums are slightly touched. This is the treatment recommended by the late Jonathan Hutchinson and it is the one which I endorse where oral medication is given. It is much superior to the protiodide pill so frequently prescribed in this country, in that it is much less liable to cause ptyalism or diarrhea. A remedy of worth in tertiary syphilis (when it cannot be treated in the proper way) is Zittmann's decoction. The formula for this has been in existence since 1765. It is composed of bichloride of mercury combined with sarsaparilla, guaiac, anise and other useless ingredients. The tannate of mercury, the initial dose of which is 0.002 gm. t. i. d., combined with extract of hyoscyamus has a well established reputation as the least liable of all the mercurials to upset the stomach. The bichloride is not infrequently combined with iodide of potassium in water and some indifferent syrup, such as sarsaparilla or orange, where the combined action of the two drugs is required. This is the so-called "mixed treatment" for late secondary and tertiary symptoms.

As an adjuvant to mercury in the treatment of syphilis by mouth the fluidextract of coca is a valuable remedy. Its beneficial actions consists in its marked tonic effect upon the heart, capillaries and nervous system in general. In anemia and cachexia and in the adynamic condition occasionally induced by mercury and potassium iodide it is an excellent stimulant tonic. It is often beneficial to those patients who are addicted to the use of alcohol.

Many physicians are in the habit of giving the protiodide of mercury in pills of 0.012 gm. (gr. $\frac{1}{5}$), beginning with one pill three times a day and continuing for several days and increasing one pill a day until the gums become slightly affected—"touching the gums" as the physicians of a former time designated it. The dose is then gradually diminished until the patient is taking one-half the amount required to produce this effect. This is the so-called average dose, which is usually three to six pills *per diem*. This should be continued—with certain intervals of rest—throughout the course of treatment. During the rest intervals, iodide of potassium may be given to eliminate the mercury stored up in the tissues, and in addition, to obtain the special eliminative action of that drug upon any morbid products.

In the event that the patient does not tolerate mercury well, extract of hyoscyamus 0.006 gm. (gr. $\frac{1}{10}$) may be added to each pill, or the tincture may be added to a mixture.

The bicyanide of mercury has been known to agree when no other preparation could be tolerated. Bismuth subnitrate in 10-grain doses t. i. d. may also be given if the stomach and bowels are restive under the influence of the drug.

If the patient is anemic and the anemia does not improve under mercury the following iron pill may be given.

℞—Sodii arsenatis	0.03–0.06 gm.	½–1 gr.
Ferri reducti	2 gm.	30 "
Pulv. rhei	4 "	1 dr.

M. et pone in caps. No. xxx.
Sig.—One capsule three times a day.

The mercury may be embodied in this capsule; or strychnine may be added. Cod-liver oil and other fatty emulsions may be given if the patient's condition so demands.

In the treatment of syphilis by mouth there are times when mercury and potassium iodide are best withdrawn and the patient treated with general tonics and a change of air, and rest. Hence it is well at times after the drugs—mercury and potassium iodide—had been given until the patient begins to show the effects of too much absorption, to withdraw them altogether and institute a course of tonics amidst the best surroundings available, after which a return to specific treatment may again be resorted to.

Lesions of the nervous system, if gummatous, require high doses of potassium iodide, if arterial, high doses of mercury, for short periods with intermissions for hygienic treatment. In the treatment of nervous lesions it must always be remembered that treatment must continue even after the lesions have improved or disappeared. This holds good, I may say, in the treatment of all the lesions of syphilis by oral administration.

Early cephalagia and neuralgia are best treated with potassium iodide. The same is true of gumma no matter where the location. Mercury may also be given to prevent relapse.

During a course of mercurial treatment, the patient should abstain from all food that is strongly acid. Fresh fruits especially should not be eaten while the patient is taking mercury.

In thus briefly reviewing the treatment of syphilis by oral administration of the specific mercury and potassium iodide I do not wish the reader to infer that I recommend the treatment of syphilis in this manner. I emphatically do not. At the present time it is at best but a poor makeshift for methods that are infinitely superior. However, it is given here because I realize that circumstances may in some instances prevent the patient from being treated properly and since he has at least to receive some treatment, which in all probability would be by mouth, I have detailed the oral treatment of the disease.

The following prescriptions will be found to be among the best that can be used for the oral administration of mercury and potassium iodide.

℞—Hydrargyri biniodidi	0.12–0.24 gm.	2–4 gr.
Potassii iodidi	2 gm.	30 "
Tincturæ cinchonæ comp. . .	105 cc	3½ oz.
Aquæ . . . . . q.s. ad	120 "	4 "

M.
Sig.—A teaspoonful three times a day in a wineglass of water after meals.

(In this prescription the iodide serves to render the mercury soluble. It serves no other purpose.)

℞—Hydrargyri bichloridi	0.06–0.12 gm.	1–2 gr.
Tincturæ cinchonæ comp. . .	60 cc	2 oz.
Aquæ . . . . . ad	120 "	4 "

M.
Sig.—One or two teaspoonfuls three times a day after meals.

℞—Massæ hydrargyri	0.12 gm.	2 gr.
Ferri sulphatis exsiccati . . .	0.06 "	1 "

Misce et fiat pil. No. i.
Sig.—One pill three times day.

℞—Hydrargyri biniodidi	0.06–0.12 gm.	1–2 gr.
Potassii iodidi	15.0–30.0 "	½–1 oz.
Syrupi aurantii corticis . . .	90 cc	3 "
Aquæ	30 "	1 "

M.
Sig.—A teaspoonful three times a day after meals in a wineglass of water.
(Mixed treatment.)

℞—Massæ hydrargyri	4 gm.	1 dr.
Ferri reducti	2 "	30 gr.
Tragacanthæ		
Glycerin, āā q.s. ad.		

Misce et fiant pilulæ No. lx.
Sig.—One pill after each meal and gradually increased.

Inunction.—Mercury can be administered by inunction, that is, by rubbing the drug, combined with some fatty base such as the official unguentum hydrargyri, or as it is common called—"blue ointment." Aside from being, perhaps, the oldest method to be employed to introduce the drug into the body, it is also one of the best—if not *the* best. It has the disadvantage of being rather uncleanly, and a fastidious individual for that reason may object; but for results it cannot be equaled except by the intravenous method and this method unfortunately is not applicable to all patients. Aside from its rapid and powerful action, the inunction method does not disturb the stomach, as a rule, although at times it causes gastric and intestinal pain and diarrhea. Also, in some patients, inunction after a time causes lassitude, muscular pain and fatigue. Inunction also sometimes causes in susceptible indi-

viduals a dermatitis which may be localized where the inunctions are given, or it may become generalized over the entire cutaneous surface. In some instances it gives rise to a mercurial eczema which consists of a deep red diffuse area of erythema with confluent vesicles full of clear fluid, which later becomes turbid as it becomes infected with pyogenic organisms. Accompanying this is swelling of the skin of the affected part with heat and intense pruritus. However, it does not become chronic, but as soon as the use of the mercury is suspended and starch, or some other emollient dressing, is applied, it quickly disappears. The most common complication of the inunction method is stomatitis. The stomatitis of the present day, however, is rarely if ever as severe as the stomatitis mentioned by the older writers. Necrosis of the maxillary bones is now no longer seen, and the teeth rarely fall out unless loosened already by pyorrhea. Neglect of buccal hygiene is responsible in most cases for the stomatitis that sometimes develops.

In giving inunctions about 4 to 6 gm. of the strong blue ointment should be used. If there is any hair growing on the part of the body to receive the inunction it should be shaved off. A hot towel should be applied to the skin for a few minutes so as to render it more permeable, for I believe that the mercury is absorbed through the skin and not volatilized and absorbed through the lungs as some would believe. Each inunction should last about fifteen or twenty minutes, or until the mercury ointment has almost disappeared, leaving the surface to which it has been applied a shiny, yellowish-gray. It is best to begin on the back—on one side, then the other side, then on the chest, then on the abdomen, and then on the arms or legs. This will mean six inunctions. The patient then rests for a day and takes a hot bath and scrub to cleanse the skin. The same shirt should be worn throughout the course of treatment, thirty inunctions are considered as a course unless the patient shows signs of salivation before that time, when the inunctions should be stopped, a bath taken and the shirt changed. By wearing the same shirt the patient gets the benefit of a constant effect of the drug until such time as its use is discontinued.

Recently Cole, Gericke and Sollmann, as the result of an experiment carried out by them, have concluded that just as good results from this form of mercurial medication can be obtained if the mercury remaining on the skin after the inunction, is cleaned off with benzene. They claim that this method is equally efficacious in so far as the absorption of the drug is concerned as the old way of allowing it to remain on the part of the surface which has been rubbed. It is undoubtedly more cleanly and less liable to cause mercurial dermatitis.

Intravenous Injection.—The most potent way in which mercury can be introduced into the body is by intravenous injection. It is also the cleanest and the most accurate as well. Its only drawback is that every patient's veins do not lend themselves to this method. For instance, if the veins are small, as in women, it is practically impossible to use this method as a routine measure. It is only in individuals whose veins are prominent, therefore, that this method is applicable. Intravenous injection causes the drug to act more quickly than by any other method, and the dose can be regulated at will. When properly done it is not painful.

A solution of bichloride, benzoate, or any other soluble mercurial salt, is made up in solution so that 10 minims equals 0.006 of the drug. This is dropped by means of a medicine dropper into 6 or 8 cc of normal salt solution. A tourniquet is applied and the vein into which the solution is to be injected is made prominent, the syringe is armed with a fine hypodermic needle and the vein is punctured and a small amount of blood is allowed to run into the syringe and mix with the solution. It is then slowly injected. This can be repeated every day, or every other day, the dose being gradually increased until 0.02 gm. of mercury is being taken.

The advantage of this method is that it acts more promptly than any other and, during its administration, it is not necessary to administer potassium iodide. As it is rapidly excreted, more so than by any other method, there is no accumulation of mercury in the system and, consequently, the dangers or rather disadvantages of ptyalism are reduced to a minimum. Its disadvantage is that, unless properly done, phlebitis is apt to occur. This method was first popularized in this country by Nixon, and I desire to go on record as stating that, where it is possible, it is the method of choice in giving mercury.

Always in giving mercury it must be remembered that it is decidedly nephrotoxic. The kidneys must be watched. If albumin or casts are present its use is decidedly contraindicated. Contrary to the generally accepted opinion, however, mercury does not cause an inflammation of the kidneys—a nephritis; but rather a degeneration—a nephrosis.

Occasionally an individual is found who cannot tolerate mercury. Such cases are rare, but when such an idiosyncrasy is found it is usually when the drug is given by mouth.

No patient should be under the influence of mercury continuously. The profound anemia sometimes seen in old syphilitics is, in my opinion, not infrequently due to the ill-advised methods of prolonged use of this powerful drug. The seeming idiosyncrasy to mercury is in many instances, however, due to a bad condition of the teeth. If these are bad, a visit to the dentist is absolutely

necessary in order to prevent this distressing complication. Should the symptoms of ptyalism supervene, such as painful gums, increased salivary flow, and a foul odor to the breath, the drug should be stopped at once. The patient should be directed to wash his mouth with a mouth wash of potassium chlorate—6 gm. to 250 cc of aqua mentha piperita—and if the gums are especially painful they may be painted with a mixture of equal parts of Lugol's solution and tincture of myrrh to which is added 2 cc of tincture of aconite. Elimination should be encouraged by copious water drinking and some *non-acidulous aperient* (do not use citrate of magnesia). Iodide of potassium should be given if the patient is not already taking it—and given in large doses—20 to 30 minims of the 100 per cent solution, t. i. d. Atropine sulphate, in doses of 0.0003 t. i. d. is also beneficial. While the patient is under the influence of mercury, all foods of an acidulous nature should be prohibited, as when these are not taken ptyalism is less likely to occur.

Potassium Iodide.—Potassium iodide is the third drug in the syphilitic therapeutic triad. This drug was first introduced by Wallace, of Dublin, in 1819, and was first used for the treatment of syphilis by the great French syphilologist, Ricord. Its congeners, sodium, ammonium and rubidium iodide, may be mentioned in passing, as they are sometimes, although rarely, used. There are also various proprietary preparations containing more or less iodide, which are sometimes used as substitutes for the potassium salt. It is claimed for them that they do not disturb the stomach or cause symptoms of iodism. I have never been able to discern their vaunted superiority. Potassium iodide has no action on the Treponema pallidum as such, but the morbid products caused by it are modified and eliminated through its action; and this is done by promoting fatty degeneration and absorption of the imperfectly organized exudates. For that reason, iodide of potassium is of value only when these new growths are still in the active stage. When they have changed into fibrous tissue the iodide exerts no action upon them, and for that reason in old fibrotic processes the drug has no effect. To give iodide in these cases, as is often done under the mistaken idea that they can be absorbed through the action of the drug, is to do no more than to derange the patient's stomach. In the early stages of syphilis, when the disease partakes more of the character of an eruptive fever, iodide is of little use. Its therapeutic efficiency increases, I may say, in direct ratio with the age of the disease. This is because in tertiary syphilis the tendency is toward new formations composed of exudates and upon these iodide exercises a potent effect. An exception to this is in congenital syphilis. In these cases potassium iodide should be exhibited at once in conjunction with mercury.

Potassium iodide must be exhibited in large doses, if satisfactory results are to be obtained. My plan is to give ascending doses, beginning with 10 grains (0.6 gm.) t. i. d., and increase the dose by 1 grain (0.06 gm.) per dose each day until the patient is taking from 30 to 40 grains at each dose. I usually have the drug given in 100 per cent solution and administered in carbonated water, either immediately before or after meals. Like mercury, potassium iodide should not be given continuously. A course of iodide medication should not extend over five weeks. Potassium iodide should be given well diluted. It should not be given combined with any other drug—simply in carbonated water or milk. For its incompatibilities I would refer the reader to a work on therapeutics.

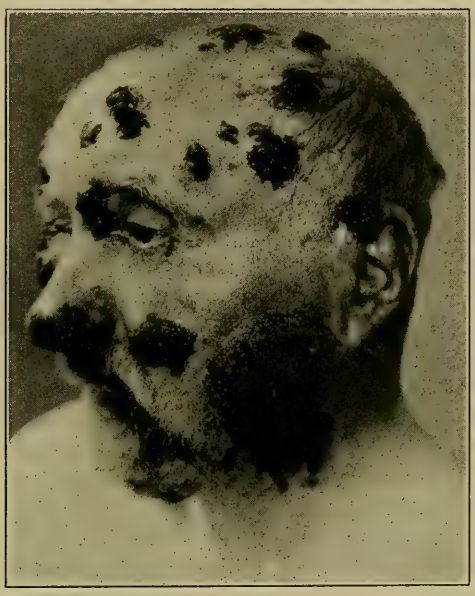


FIG. 57.—Iodide rash. (Courtesy of Dr. M. Shapiro.)

Potassium iodide is rapidly eliminated through the saliva and the urine, but some of the drug when exhibited in large doses tends to accumulate in the body. For that reason, after ten days of the maximum dose it should be gradually reduced to half of the initial dose and so continued until the course of iodide medication is concluded. In this way the eliminative or alterative effect is maintained without too much disturbance to the gastric mucosa.

Iodide Grippe.—In some persons taking potassium iodide, symptoms resembling coryza, the so-called "iodide grippe" appear. There is also a tendency during the exhibition of the drug for an acne

eruption on the face, chest and back to appear. Others show their idiosyncrasy to the drug by the symptoms of gastric irritability or mental depression. In those specially susceptible, sudden and dangerous edema of the glottis may appear. These symptoms may all in a measure be prevented by the simultaneous administration of calcium lactate, or sodium bicarbonate, or a few drops of tincture of belladonna may be added to each dose.

Should the symptoms of iodism appear, and there is urgent need for its administration to be continued, do not diminish the dose but, on the contrary, increase it; for, strange to say, this procedure almost invariably causes the distressing symptoms to pass away.

Never give potassium iodide in pill or capsule. The addition of stillingia to enhance its action is not worthy of consideration. Modern therapeutic knowledge has proven that vegetable alteratives are practically worthless in the treatment of syphilis.

Sodium Iodide.—Sodium iodide can be given intravenously and in very massive doses. Howard has given as high as two hundred grains at a dose. A 5 to 10 per cent solution should be made, and this added to sterile distilled water and injected. I have not used this treatment, as I believe the same effect can be reached with arsphenamine much more quickly and accurately than by using the iodide in this manner. I do not, therefore, recommend its use.

Having discussed the therapeutic agents used in the treatment of syphilis, and their manner of application, I will now take up the treatment of syphilis in detail.

Treatment Must Be Vigorous.—In treating syphilis, I wish particularly to emphasize the necessity of vigorous treatment. While it is undoubtedly true that there are cases which sometimes recover (and by recovery I mean that a positive Wassermann is changed to a negative and remains so) even under very indifferent treatment, yet in the vast majority of instances the more vigorous the treatment is, the quicker and more lasting will be the results obtained. Success in the treatment of syphilis can be summed up in the words of the great Fournier, "Strike hard, quick, and often." There is no disease which responds so readily to specific treatment as syphilis and, paradoxical as it may seem, there is no disease which so often goes uncured. The reasons for this, in my opinion, are the lack of persistency on the part of the physician, and the lack of persistency on the part of the patient. While there are few, if any, physicians who do not realize that the cure of syphilis is often a long drawn out affair, yet when the patient's symptoms have subsided they not infrequently let him go; or else they treat him inadequately from the beginning. When the patient is at fault—as in truth most times he is—it is almost invariably because he feels so well from the treatment received that he fails to realize the necessity of continuing treatment until the disease is entirely eradicated—that is, when he is permanently Wassermann negative.

Chancre.—Let us first consider the treatment of syphilis in the primary stage—when the patient first seeks medical advice because of the appearance of the chancre, which few fail to do, if the sore is sufficiently noticeable to attract attention. It is during this stage that the best chance is offered for a quick and permanent cure. The disease, as yet, has not made a profound impression on the tissues; the treponemata have not had time to migrate to inaccessible tissues, or if they have, they have not had sufficient time to increase to such an extent that their total destruction is impossible. It is the psychologic moment, as it were, in the treatment of the disease, and he who hesitates is lost; for, as Fordyce truly says, the first six months is the most important period in the treatment of acquired syphilis. Personally, I would even lessen the time and say that the first six weeks is the most important period in the treatment of acquired syphilis. To quote Elsner, "But few, thoroughly treated during the initial and secondary stages of syphilis, develop tertiary lesions." The statistics of Neisser, Fournier, Haslund, Ehlers, Neumann and Schlotz confirm this. The importance of proper diagnosis and treatment in this stage of the disease is, therefore, supremely momentous to the patient's future health, happiness and industrial efficiency.

Excision.—Assuming that a correct diagnosis has been made, the first step in the radical cure of the disease is to excise the chancre. I am well aware that this procedure will be contested by some who state, and with truth, that the disease is not arrested thereby. Nevertheless, I am assured that the removal of the chancre profoundly modifies the future course of the disease, causing it to be milder and more amenable to treatment. In view of the fact that the expediency of this procedure is disputed, it may not be out of place for me to digress sufficiently to explain the reason why this should be done.

The Treponema pallidum is an anaërobic organism and, therefore, when entering the body prefers the lymph channels rather than the blood stream, although it cannot be denied that it is found there also. At the point of its entrance into the subjacent lymph spaces a colony is soon formed which gives rise to a dense, nodular, round-cell infiltration, which is oxygen tight, as it were. The blood supply is shut off and, in consequence, the center of the nodule necroses and an ulcer is formed. With the development of the initial lesion, the lymph nodes adjacent thereto slowly indurate as the infection advances. As most chancres appear on the penis, the lymph nodes involved are those of the groins—the so-called "pleiades of Ricord." Thence the natural course of the infecting organisms would be into the iliac lymphatics and the receptaculum chyli. It is also to be understood that some of the organisms pass into the blood stream

and are not confined wholly to the lymphatics. This advance of the treponemata is slow. Weeks, and sometimes months, elapse before the symptoms of a generalized infection are manifest. It is not until then that a positive Wassermann can be obtained. For that reason a negative Wassermann does not preclude syphilis if the blood is taken in the primary stage or within three or four weeks of the appearance of the chancre.

From the foregoing facts, it can be readily appreciated that the chancre as the original nidus—the manufacturing center, as it were —is the place where, for a considerable period of time, the infecting organisms arise. The removal of the chancre as soon as it is recognized is, therefore, a rational procedure based upon a correct pathology.

If it is not possible, for any reason, to remove the chancre by excision it should be kept covered with a small piece of mercurial plaster, or a small piece of gauze on which has been spread mercurial ointment. This should be changed every day. Next to excision I have found this to be the best method to destroy the treponemata at their original point of infection. Incidentally this method of treatment will rapidly heal the sore.

Simultaneously with the removal of the chancre, or its treatment in the manner just described, arsphenamine should be administered intravenously. As previously stated, the dose of this should be 0.01 gm. to every twenty-five pounds of body weight to a man and thirty pounds to a woman. Thus, for an average sized man of, say, one hundred and fifty pounds, the dose would be 0.6 gm. and 0.5 to a woman. In not less than eighteen hours, or longer than twenty-four, the patient should receive another intravenous injection of arsphenamine, this time 0.01 gm. less than the first. Allowing a similar length of time to elapse, a third intravenous injection of the same strength as the second should be given. So the patient receives three intravenous injections of arsphenamine on three consecutive days.

It may seem to the reader that this is intensive treatment with a vengeance, but if we pause and consider how rapidly arsenic is eliminated from the system by the various emunctories and because of this rapid elimination how little remains after elimination, the interval, short as it may seem to be, yet is sufficient to allow the tissues to receive another dose. Also by this method the tissues, even those remote and hard of access, are constantly bathed in the spirochæticidal fluid, so that their destruction is almost inevitable. This method was first introduced by Pollitzer, and with the reasons set forth by this eminent syphilologist, as briefly stated here, I am in full accord.

In the week following the third intravenous injection of arsphen-

amine a course of mercury should be instituted. If possible the intravenous method already described should be used and the patient should receive not less than twenty such injections in as many days.

This sums up in brief an ideal treatment of syphilis in the primary stage. If carried out it will almost certainly entirely eradicate the disease. In the secondary stage, it may be necessary to repeat the course, but in most instances but one course will be sufficient. The intervals between courses should be about two months, or shortly before the Wassermann turns positive again, which usually takes about three months after the intensive treatment herein outlined, providing the case is in the late secondary or tertiary stage.

It is not possible, however, to treat every case in this manner. However, I want to insist that if any change in the treatment is made it should be in the manner of administering the mercury; and the intensive method of administering the arsphenamine should be adhered to if possible to do so. If the patient's veins will not permit so large a number of intravenous injections of mercury, inunctions are the next choice. Thirty of these should be given and during the last two weeks and for two weeks thereafter iodide of potassium should be exhibited in conjunction with them. If it is not possible to give inunctions, the next method of choice is by intramuscular injection. I use some insoluble mercurial salt, such as the salicylate, or calomel, or gray oil or Lambkin's cream. From ten to fifteen minims are given at each injection at weekly intervals. Not more than five injections should be given. The injection should be made in the buttock at Galliot's point, which is found by dividing the gluteal region into an inner third and an outer two-thirds, at the intersection of a horizontal line two fingers breadth above the great trochanter. Injections may be made at this point and to the upper and outer side of it.

If these injections are not possible, rather than give it by mouth I prefer rectal suppositories, of which mention has already been made.

Local Treatment.—The local treatment of syphilitic lesions deserves only passing notice; as since they are but the outward manifestations of a constitutional disease, they quickly respond to constitutional treatment. The healing of mucous patches may be hastened if they are touched daily with a 5 or 10 per cent solution of nitrate of silver, and condylomata disappear more rapidly if dusted daily with calomel or covered with mercurial ointment spread on gauze. For the alopecia, concerning which the patient often complains, applications of mercury bichloride solution of 1 : 10,000 combined with quinine and bay rum will be found to be beneficial.

Congenital Syphilis.—In the treatment of congenital syphilis in infants, Brodie's method of applying a small amount of mild

mercurial ointment, or oleate of mercury—about 5 gm.—on a flannel binder, which is allowed to stay on for three or four days, is, in my opinion, a method which can hardly be improved upon, and it has been in use for many years. If the infant is breast fed, the mother should be treated with arsphenamine and mercury in the usual way and the infant will receive the benefit of the treatment as well. This is a most excellent method of treating infantile syphilis. Mercury and chalk powder in doses appropriate to the infant's age is also a valuable means of combating the disease. For lesions about the anus and the surface of the body, bichloride of mercury baths are very beneficial. An ordinary bichloride tablet of $7\frac{1}{2}$ grains dissolved in 5 gallons of water will make a bath of the proper strength. Care must be taken, however, that the infant does not swallow any of the bichloride solution.

In treating congenital syphilis in infants, iodide of potassium plays an important part. The dose should be in proportion to the infant's age and weight. It should not be given for a longer period than two weeks, or three at the utmost.

Arsphenamine should always be given to syphilitic infants. For infants from ten days to six weeks old 0.05 to 0.06 gm. may be given, to be repeated in from four to six days. In treating infants, I prefer to use neoarsphenamine as it requires a lesser amount of solution, which in my opinion is an advantage. Six or eight injections may be required before the Wassermann becomes negative, although the infant improves wonderfully and the symptoms disappear much sooner. Intravenous injections in infants are made in one of the veins of the scalp, which are usually sufficiently prominent to be used for this purpose. The child rests on a high couch or table with its head on a hard pillow and firmly supported by an assistant, as it is absolutely essential, in order to do the operation properly and without danger, that no movements should occur. A vein is rendered prominent by gentle pressure by the finger of an assistant, and the needle is gently pushed into the vein and the solution injected, a fine hypodermic needle being used. Occasionally the veins at the bend of the elbow are sufficiently prominent to be used.

In older children the method of treatment is the same as in adults, except as to the dosage of the specific drugs.

Nervous Syphilis.—Until quite recently the treatment of the graver forms of nervous syphilis has been on the whole unsatisfactory. This has been due partly to a lack of knowledge as to the causes of these conditions and partly to insufficient therapeutic weapons, or rather to the non-application of the same. These defects have within the past twelve years been remedied in part at least by the discovery of the cause of syphilis and the part it plays in the pro-

duction of many pathological states which formerly were not considered to be of syphilitic origin, as for instance tabes and paresis, and also by the discovery of arsphenamine and its rapid and profound effect upon the causative organism. In 1912, Swift and Ellis of the Rockefeller Institute devised the method of intraspinal injections of salvarsanized serum, which marked a notable advance in the treatment of syphilitic lesions of the nervous system. Their method has since been modified by Ogilvie, Wile, Hunt, and others. Although condemned by some, it has produced excellent results with the prospect of further improvement in the future. This method is applicable to all forms of syphilitic diseases of the nervous system.

In the treatment of these conditions, however, there are certain factors which must be considered in order to reach the maximum of success; these are discussed in the chapter on the Serology of the Disease.

Intraspinous Treatment.—In giving arsphenamine or mercury intraspinously, the following technic is to be employed. The patient is given a full dose of arsphenamine intravenously, and half an hour later 60 cc of blood is withdrawn and collected in a McRae tube. This blood is slanted and allowed to stand at room temperature for at least twelve hours—it may take eighteen hours for the serum to completely separate from the clot. This supernatant serum is now pipetted off and centrifuged for at least a half an hour, or until the red blood cells have been completely precipitated at the bottom of the tubes and the serum is clear and free from blood cells. Should it hemolyze, under no circumstances should it be injected. The serum is then placed in a thermostat and inactivated by keeping the thermostat at a temperature of 56° C. for half an hour. The serum is now ready for injection into the spinal canal, with the exception of adding 3 to 4 mgms. *i. e.*, three or four drops of arsphenamine solution, which should be done immediately before it is to be injected. This last is a reinforcement suggested by Fordyce, and one which I commend. A lumbar puncture is made on a level with the crests of the ilia. This corresponds with the tip of the fourth lumbar vertebra. It may be made higher, between the third and fourth lumbar vertebra, or lower, between the fifth lumbar and the first sacral vertebra. The patient should be lying on his side with his knees drawn up and his face resting upon them, so as to separate the intervertebral spaces as much as possible. A puncture with a scalpel may be made, but as a rule this is not necessary. The left thumb or index finger is placed between the spinous processes as a guide and the needle is slowly pushed through the tissues on the same level as the finger, but about one-half inch (1 cm.) from the median line, in an upward and inward direction. A certain lessened

resistance will inform the operator when the spinal canal has been entered. As soon as the canal is entered the stylet should be withdrawn and the fluid will at once flow. A manometer may be attached to determine the pressure, which in the exudative stage of tabes and in cerebrospinal syphilis is sometimes considerable. As much fluid should be allowed to flow out as will equal the amount of serum to be injected. A small rubber tube is now attached to the needle and to the syringe and the solution allowed to run in by gravity. The needle is then withdrawn and the wound sealed with collodion or a dry dressing applied. I do not advise the use of local anesthesia, as I have never found the operation sufficiently painful to necessitate it. After the operation, the patient should remain in bed for several days, as otherwise an intense headache may develop along with dizziness and vomiting. In very many cases there is a sharp reaction characterized by shooting and lancinating pains in the legs and arms and a headache of marked severity. These pains may be so severe as to warrant the use of morphine. They are supposed to be of an anaphylactic character and some believe that they are of bad prognostic import. I cannot say that I have found this to be so in every case. Sometimes a dry puncture is made. This may be due to the needle not entering the canal, under which circumstances it might more properly be called a mis- or false-puncture, or it may be due to a clogging of the lumen of the needle because of increased viscosity of the fluid. It is more apt to occur after repeated punctures have been made.

These treatments should be given at intervals of about two weeks. If successful, an improvement will be noted in a few days following the injection.

Ogilvie of New York has modified the original Swift-Ellis method as follows: From 50 to 60 cc of blood is withdrawn without any previous administration of arsphenamine. This is immediately centrifuged and 15 cc of the supernatant serum is pipetted off. To this is added 4 cc of a solution of arsphenamine, which is made up in the proportion of 0.25 mg. of arsphenamine to 1 cc of normal salt solution, care being taken that the arsphenamine solution and the serum are mixed at exactly the same temperature. The mixture is then placed in a thermostat at a temperature of 37° C. for forty-five minutes and then for thirty minutes longer at 56° C. It should be injected at once.

The method of Ravant is to do a lumbar puncture and allow about 10 cc of spinal fluid to run into the syringe. To this spinal fluid in the syringe is added two or three drops—not more—of an arsphenamine solution made up in the usual way. When the arsphenamine solution is added it is mixed with the spinal fluid in the syringe by means of a small glass rod. The mixture is then allowed to flow

back into the canal. This method does not commend itself to me and I do not advise its use.

Intraspinous Administration of Mercury.—Mercury can be administered intraspinously by adding 0.001 to 0.002 gm. of bichloride or benzoate of mercury suspended in 2 cc of normal salt solution to 15 cc of serum obtained after the manner already described. The mixture is inactivated in a thermostat at 56° C. for half an hour and injected as soon as possible thereafter. In passing I might add that the proper amount of mercury may be obtained by adding to the salt solution two or three drops of the stock solution used in the intravenous injections already described.

E. Livingston Hunt of New York has devised an excellent and simple method of injecting mercury intraspinously, and one which is so simple that it can be easily and quickly prepared. To 4 cc of normal salt solution 0.002 to 0.003 gm. of mercury bichloride is added and injected. I have used this method many times and can vouch for its efficacy.

Mercurialized serum or solution should be injected not oftener than once in seven or eight days, or rather less than the interval required for arsphenamine injections. The reaction is not so severe as when the latter drug is used. In the treatment of syphilitic iritis, where arsphenamine is often contraindicated, especially if the inflammation is severe, intraspinal injections of mercury can be used in the beginning until the condition is sufficiently controlled to warrant the use of arsphenamine. It is well to remember this, as the indiscriminate administration of arsphenamine in acute conditions of the optic nerve is sometimes followed by unpleasant consequences.

In 1913 Levaditi and Martel experimented with rabbits by trephining them and injecting auto-salvarsanized serum into the ventricles. The treatment would seem rational and the procedure has been done a number of times for paresis. The results, however, have not been sufficiently encouraging for me to attempt it, and I do not advise its use. It is possible that improved technic may later show results that will make it worth while.

Of all the diseases which afflict mankind, none are so protean and oftimes so fearful, and yet so amenable to treatment, as syphilis; and—at the same time—none so refractory. The reason for this is that too many physicians fear to use the instruments at their hand. They give, it is true, arsphenamine, mercury and potassium iodide, but they do not give them often enough. Then they wonder why their "specifies" are not specific. If I may be allowed to individualize such an elusive and incorporate an entity as a disease, I would say: In fighting syphilis you are fighting a dangerous and a crafty foe, a foe who shows no mercy and to whom no mercy

should be shown; a foe of many resources; one, who when he seems beaten and utterly overthrown is still engaged in rallying his forces in some hidden, secret fastness to venture forth again when the time seems ripe to ravage and destroy. With a strong hand and an outstretched arm should such a foe be smitten. Do not hesitate, do not be afraid, do not defend. Attack, always attack, never wait, but ever march to meet the enemy at the gate. So will you conquer syphilis.

CHAPTER XVII.

THE UNTOWARD EFFECTS OF ARSPHENAMINE.

The untoward effects of arsphenamine are either immediate or remote. That is the patient shows the effects during or immediately following the injection of the drug or they may be delayed for several days or even a week. They may be so slight as to be hardly noticeable by the patient or the physician, they may be simply unpleasant, or they may be so severe as to be extremely alarming, or they may result in death.

When we consider the millions of times and the variety of practitioners who have administered arsphenamine it is very evident that these untoward effects are not frequent. The administration of arsphenamine is no more dangerous to life than the administration of ether and yet occasionally deaths occur from ether anesthesia; and the same is true of arsphenamine. I do not believe that arsphenamine *per se* if properly administered is dangerous to life. If it were as dangerous as some assume its death toll would be immeasureably greater than it is. When we consider the number of injections that have been given and the deaths that have occurred it can readily be appreciated that this danger is almost infinitesimal. That danger exists however, is undoubtedly true; but, as pointed out by Ehrlich, it is to be found in the patient himself, not in the drug. In other words where the danger lies is in how the patient reacts to the drug, not in how the drug reacts to the patient. In most instances it is possible to anticipate the danger; in some cases (and these are usually those which are unpleasant rather than dangerous), it is impossible.

To anticipate the danger is not difficult; on the contrary, it is quite easy. It consists simply in *a careful examination of the patient to discover if any defects exist that would render the giving of the drug dangerous to life, and also precautions to prevent colloidoclasis.* The last is the unknown element that must always enter into our calculations.

Colloidoclasis.—Let us first consider death following the immediate use of the drug; that is occurring during its administration or immediately thereafter or within twelve hours. A review of the literature shows that death within the time period mentioned has followed both old and new arsphenamine, that is the drug containing the greater as well as the less amount of arsenic. It has occurred

in the infantile and the senile, in those in seemingly perfect health and in those desperately ill. It has occurred with the most eminent operators as well as with the most mediocre. But, as Wechselmann very properly points out, investigation is to be directed not toward those patients who, before treatment, were affected with some grave organic disease, but rather toward those who were seemingly healthy and where there was no error in the technic of administration. It is these cases which change a simple and supposedly harmless procedure into a sudden and overwhelming catastrophe. What causes death then in those patients who come to the table seemingly sound and strong? It can be answered in one word—*colloidoclasis*. It would be more accurate however if I used instead the term "medicinal intolerance." It is this individual idiosyncrasy to organic arsenic that causes the serious and sometimes fatal symptoms to develop suddenly in a patient in whom there is no discoverable organic defect. It is not my purpose here to discuss the theoretical causes of colloidoclasis. Milian is of the opinion that it is due to adrenal insufficiency. This is possible, but I am in accord with the view of Lumière and Kopaczewski that the colloidoclasis sometimes seen when organic arsenic is injected into the blood stream is due to flocculation in the serum and a change in the electric charge of the colloids in the serum. The physical balance is thereby upset, and the flocculation obstructs the capillaries thus causing a fulminating asphyxia of the tissues. As to the more remote effect —the toxiderma sometimes seen—the "arsenic rash"—I am in accord with Darier that t represents a cutaneous chemical traumatism, and is due to an idiosyncrasy of the skin itself.

Colloidoclasic Shock.—These symptoms of colloidoclasis have been likened by Milian to the crises caused by an overdose of amyl-nitrite and for that reason have been designated by him as "nitritoid crises." Girbal would even make a distinction between anaphylactic or colloidoclasic shock and "nitritoid crisis." In the light of present knowledge I do not believe this distinction to be tenable. While the arsphenamine is being injected or shortly afterward, the patient begins to cough; and when coughing occurs during the administration of the drug the physician should always pause and look at the patient's face, which becomes red and suffused. The face swells and becomes cyanosed, the tongue protrudes and the lips swell, the eyelids are also swollen and the pupils are dilated. The patient becomes unconscious and the breathing becomes shallow and stertorous, the pulse thready and weak. All of these alarming symptoms may develop and the patient be dead within five minutes. This is the "crisis of the first degree" of Danysz. Alarming and fulminant as it may seem the patient sometimes recovers—more frequently he dies. In the less severe cases there is

flushing of the face, dyspnea, rapid pulse and prostration; within half an hour however, the patient is normal again, except for the fright of his experience. In some cases the only evidence of colloidoclasis is a slight flushing of the face.

Colloidoclasis rarely occurs with the first injection. It sometimes occurs with the second; it is most frequent with the third; rarely it occurs with the fourth. It is most apt to occur if the patient has eaten a full meal shortly before the injection; for that reason, arsphenamine should always be administered on an empty stomach—five hours at least should elapse after a meal before an injection is given.

Adrenalin.—Assuming that adrenal insufficiency was the cause of these alarming symptoms Milian long ago advocated intramuscular injections of adrenalin 0.3 cc five minutes before the arsphenamine is to be given. Adrenalin, however, has no power to prevent the hemolysis which is the essential feature of the shock following the intravenous injection of organic arsenic. The asphyxia observed in this form of shock is in no way influenced by adrenalin since this drug while acting most powerfully upon the vascular system in general yet exempts the *pulmonary* vessels from its vasoconstrictor effects. It has also been shown by Auer and Lewis and also by Manwaring and Crowe that in the asphyxia caused by colloidoclasic shock the spasmodic contraction of the bronchioles plays almost as important a part as the hemolysis in the pulmonary capillaries. Atropine rather than adrenalin is therefore the logical drug to use. It is the method of prevention that I personally employ. Recently however, Sicard and Paraf, working on the theory of Lumière and Kopaczewski of flocculation of the serum following the introduction of arsphenamine into the blood stream, have preceded it with 30 cc of normal saline solution to which has been added 0.6 or 0.75 gm. of sodium carbonate. They claim that this protects against the anaphylactic shock of arsphenamine, more effectually than adrenalin.

During an attack atropine should be given hypodermically, also some form of digitalis that can be injected subcutaneously such as digipuratum or digalen. Camphor in oil may be used. Oxygen is of value.

Besredka Technic.—A method that is employed by Stokes at the Mayo clinic to prevent anaphylaxis is the so-called "Besredka technic." It is simple and efficient. The dose of arsphenamine to be given is divided into two doses, one of one-tenth and the other of nine-tenths. One hour before the larger dose is to be given the smaller dose is given and forty minutes thereafter one-fiftieth of a grain of atropine is injected hypodermically. Twenty minutes later the larger dose of arsphenamine is injected.

I have not as yet employed this method of preventing anaphylaxis but coming as it does from such an eminent authority I am quite convinced of its efficacy.

Danysz advises a small preparatory injection of 2 to 4 cc of the arsenical to be used, several hours before the maximum therapeutic dose is to be given. Kolle, the successor of Ehrlich advises a dose of one-fifth to one-fourth of the therapeutic dose to be injected twenty-four hours before.

Occasionally after the injection of arsphenamine a widely disseminated, bright red rash appears—the so-called "arsenic rash." It can be distinguished from the Jarisch-Herxheimer reaction in that it appears several days to a week after the injection, although rarely it may occur within twenty-four hours. It fades within a week and requires no local or constitutional treatment. It indicates that the patient in whom it appeared is sensitive to the drug and therefore more than usual caution should be exercised in its administration. If one or two injections cause the eruption the drug should not be given again until several months after the complete disappearance of the rash. Even after this lapse of time, the possibility of acute yellow atrophy of the liver developing must always be remembered.

Sudden death has followed the giving of arsphenamine in severe cardiac disease—especially fatty degeneration or myocarditis. The danger in cardiac disease is however, in my opinion, comparatively slight if neoarsphenamine or silver salvarsan is used, which allow the drug to be given in as low as 15 to 30 cc of water. Under no circumstances in the presence of cardiac disease should old arsphenamine in a dilution of 300 cc of water be used.

Diseases of the upper air passages, bronchitis, acute or chronic, asthma and bronchiectasis should preclude the use of old arsphenamine. Neoarsphenamine or silver salvarsan in low dilutions can however, in my opinion be given with impunity. Drug addiction is an absolute contraindication to the giving of arsphenamine. From personal experience in a large penal hospital in which quite a number of the syphilitics were also drug addicts I can say that these patients are those who are most apt to develop symptoms of anaphylactic shock. Patients with syphilis who are also drug addicts should not be treated with arsphenamine intravenously for at least two weeks after cure of the drug addiction.

Status Lymphaticus.—In the constitutional anomaly known as the status lymphaticus, organic arsenic must be given with great caution. The intensive treatment should never be given, nor should old arsphenamine; neoarsphenamine or silver salvarsan should be used and always in low dilution. These patients are either very tall or very short. The head may be large or small and frequently shows malformations. In males there is a tendency toward the

feminine configuration—rounded limbs, broad hips, absence of beard. In females the tendency is toward the male configuration—narrow flanks, coarse hair, which is abundant on the chest and extremities. The thyroid in these cases is nearly always enlarged and the lymphatic apparatus also. These patients almost invariably have that complexion that is usually described as "pasty" and their general appearance can best be described as "flabby." *Be very careful* in giving arsphenamine to these patients. See to it that precaution is taken to prevent anaphylaxis; be prepared if it should occur.

Encephalitis Hæmorrhagica.—In some instances the condition known as acute hemorrhagic encephalitis develops after the administration of arsphenamine. It occurs most often in those patients who have had prolonged or intensive treatment with mercury previously to being given arsphenamine. For that reason mercury should not precede arsphenamine; it should always follow it and at an interval of not less than a week. The cerebral symptoms following the administration of arsphenamine resemble very closely those of uremia and I am convinced that they are primarily due to a process that is essentially renal. Contrary to the generally accepted opinion, mercury is much more nephrotoxic than arsphenamine and if these organs have been already injured by mercury and then are insulted by arsphenamine it can be readily appreciated why this condition develops. It is only strange in view of the fact that mercury and arsphenamine are so often given together as it were, that this dangerous sequel of arsphenamine administration does not happen more frequently than it does. In a letter to the *British Medical Journal*, Ehrlich dwelt particularly on encephalitis hæmorrhagica. The principal pathologic feature of this condition of acute wet brain is a colossal dilatation of the cerebral vessels which gives rise to edema and perivascular bleeding. The vascular system, although altered by the relapse of endotoxins is not especially sensitive to arsphenamine as such, else these symptoms would show at a much shorter interval than they usually do. This delay shows very plainly that a derivative of arsphenamine of an extremely toxic nature has been formed in the meantime.

This toxic substance is undoubtedly an oxidation product—paraminophenylarsenoxide. Its formation is favored by any cause which delays the excretion of the drug—an overdose, or impaired kidneys. This prevention of elimination causes a large amount of arsenic to remain in the tissues which oxidizes. It is also possible that a certain amount of adrenalin insufficiency—not enough to induce acute anaphylaxis—may act as an accentuating cause, adrenalin being the regulator as it were of the vasodilator nerves. Again, it is possible that syphilitic involvement of the central nervous

system—which may be asymptomatic—may also help to produce the condition.

Hemorrhagic encephalitis as a rule comes on after the second or third injection of arsphenamine. For a day or two thereafter the patient may not complain. The first symptoms as a rule of which the patient complains are headache and a feeling of malaise. There is a constant sensation of nausea which is unrelieved by vomiting. The bowels are loose. The patient goes to bed and sooner or later sinks into a stupor from which he cannot be aroused. Convulsions occur. The pulse is usually full and strong. Ophthalmoscopic examination will usually reveal choked disk. There may be conjugate deviation of the eyes. Should vomiting occur at this stage it will be the characteristic projectile vomiting of cerebral involvement. There is complete or almost complete suppression of urine.

Sometimes convulsions occur in rapid succession and the patient may die in one. Usually however the coma deepens, the action of the heart becomes changed from a full and rhythmic pumping to a weak and arrythmic beating. The pulse becomes irregular, fast and thready. Within forty-eight hours or less, death occurs.

In the treatment of this most unfortunate occurrence there are two objectives which must constantly be in the mind of the physician if a cure is to be effected. These are to overcome the intracranial pressure and to stimulate the kidneys to functionate. To overcome the intracranial pressures two procedures are necessary. These are lumbar puncture and phlebotomy. Lumbar puncture should never be omitted; it is not only a therapeutic measure of great value but it is also a means whereby an accurate prognosis can be made. From 10 to 30 cc of the cerebrospinal fluid should be withdrawn. If examined for urea it will be found to be increased and if this increase is between 0.1 and 0.2 per cent the prognosis should be guarded; some of these patients die. When the increase is above 0.3 per cent a fatal outcome almost invariably occurs. The estimation of the urea can be done at the bedside. To 5 cc of cerebrospinal fluid are added 25 cc of a 40 per cent potassium hydrate solution and 2.2 cc of bromine and the result is read in a Doremus ureometer.

If for any reason it is impossible to do a lumbar puncture and thus directly relieve the intracranial pressure, venesection should be resorted to and from 200 to 300 cc of blood should be withdrawn. If however, the pulse is weak and irregular, or if the patient is anemic or senile, phlebotomy should not be done; since these patients are apt to develop thrombosis in any event and bleeding may precipitate the process.

Blood may also be deflected from the brain by purgation and for that reason croton oil in a dose of two drops in fifteen drops of glycerin may be given on the back of the tongue.

A cold pack with an ice bag on the head is also beneficial in lessening the tendency toward convulsions and promoting diaphoresis and thus reducing arterial pressure.

To stimulate the renal function there is nothing more efficacious than hot rectal irrigations. A long rectal tube should be used and not less than a gallon of water to which is added an ounce of sodium bicarbonate. Fischer's solution may be used instead; the formula of this is:

Sodium carbonate	10 gms.
Sodium chloride	14 gms.
Distilled water, to make	1000 cc.

Dry cups over the loins, or a poultice of digitalis leaves and flaxseed meal can also be tried.

Stimulants, such as alcohol, strychnine, digitalis, and camphor should be given hypodermically when the heart begins to flag.

Occasionally these patients recover. As I have just pointed out the prognosis can be accurately determined in almost every instance by an examination of the urea content of the cerebrospinal fluid.

Jaundice.—A complication sometimes following the administration of arsphenamine is jaundice. In rare instances it may prove fatal. It usually comes on within a week after the drug has been given but it may be delayed for several weeks thereafter. There is a prodromal stage lasting for several days before the icterus appears, consisting of attacks of vomiting, anorexia, headache and sometimes diarrhea. The icterus may be very intense or it may be only moderate. The stools are of the usual putty color seen in this condition when due to another cause. Pruritus is present when the icterus is established and there is also the characteristic bradycardia. The liver is enlarged and tender. The urinary findings are usually negative except for the presence of the bile pigments, bilirubin and biliverdin. The icterus may persist for several weeks or as long as two months, and recovery is complete. Occasionally, however, death may ensue with symptoms pointing to acute yellow atrophy of the liver. The jaundice deepens, vomiting becomes uncontrollable, dyspnea and delirium appear, purpura is common, lethargy is followed by coma in which the patient dies. It may take several weeks for all of this to occur.

When examined at necropsy the hepatic lesions will be found to consist of fatty degeneration and necrosis of the liver cells and they are undoubtedly due to the direct toxic action of the arsenic. To be a trifle more definite it may be said that the pathology of the condition is a diffuse intralobular hepatitis. Aside from the jaundice following the first injection of the drug which may be attributed to a Jarisch-Herxheimer reaction and which is due to the toxic action of

the Treponema pallidum stimulated to greater activity by the single dose of arsphenamine, the icterus which sometimes follows the administration of this drug is due to one of two predisposing causes acting in conjunction therewith. One of these causes is preëxisting hepatic syphilis. This hepatic syphilis is that of the secondary stage in which the degeneration of the hepatic cells is due to an acute spirochetosis of the organ. The condition just described does not follow after the treatment of gummatous hepatic lesions. To the liver cells already irritated, or perhaps already undergoing degenerative changes, is superadded the toxic action of the arsenic. The result in some instances is a more or less severe icterus. The other cause is where the patient has previously been treated, either intensively or for a prolonged period, with mercury. As recently stated by Schamberg—"The pathogeny of such poisonings is reasonably clear. Mercury in vigorous dosage, particularly when the insoluble salts are used, may severely irritate the kidneys and inhibit their power to eliminate arsphenamine. Within a short time after an injection of arsphenamine most of it disappears from the blood and is lodged in the organs, one of the chief reservoirs being the liver. If the eliminatory activity of the kidneys is impaired it is obvious that the arsphenamine will remain for a longer time and in larger quantities in the liver, for which organ it has a considerable affinity. Too long a residence in the liver may cause the drug either to become oxidized with the production of arsenoxide, or the arsenical radical may become split off and produce the symptoms of arsenical poisoning."

Not a few of the so-called Jarisch-Herxheimer reactions characterized by jaundice which occur after a single dose of arsphenamine, can be traced, in my opinion, to a renal injury due to previous treatment with mercury.

The treatment of these cases is rest in bed and free catharsis with a saline. During the acute stage the diet should be exclusively milk and carbonated water. Later a bland vegetable diet may be given. An intramuscular injection of intramine—3 cc should be immediately given as intramine is a specific for poisoning with metallic substances. This injection should be repeated in three days, and one week later 5 cc should be given. Rectal irrigations with cold saline solution, using about a gallon at a time should be given daily. Other symptoms should be treated symptomatically.

Arsenical jaundice is a comparatively rare occurrence. According to Harrison it occurs in 0.6 per cent of cases of syphilis during or subsequent to treatment with arsphenamine. I am inclined to accept this as correct from a study of the reports of other observers both in the United States and Europe.

This chapter would not be complete without also considering the

poisonous effects sometimes observed when the other two specifics for syphilis are exhibited—mercury and potassium iodide.

If arsphenamine has an affinity for the liver, mercury can be said to have an equal affinity for the kidneys. If given in excess it can and does produce degenerative changes in the kidneys similar to those produced by arsphenamine in the liver. For that reason in the presence of nephritis as evidenced by albumin and casts in the urine whether due to the syphilitic disease or not, mercury should not be given. In the event of nephritis arising during the course of treatment with mercury intramine should be given as described above, and in addition the anuria should be combated with hot rectal irrigations, hot poultices of digitalis leaves and flaxseed, or dry cups, over the loins. The treatment is practically the same as that for uremia which has already been described.

When used externally mercury sometimes produces an acute dermatitis. This may resemble very closely the eruptions of measles or scarlatina. It may also be macular, urticarial, purpuric or pemphigoid. It is worth while knowing however, in this connection that the eruptions produced by mercury in no way resemble those due to syphilis, except perhaps when the eruption is macular. These mercurial dermatoses rapidly resolve as soon as the drug is discontinued. Occasionally soothing lotions or ointments may be applied to hasten this or to allay the irritation.

Stomatitis or ptyalism is discussed in the chapter on Treatment.

Potassium iodide sometimes produces symptoms not unlike those of acute coryza—running of the nose, lacrimation and edema of the eyelids. In rare instances it may produce edema of the glottis. Not infrequently it produces an acneiform eruption on the chest and back—especially the latter. A more detailed description and the treatment of the same will be found in the chapter on Treatment.

The untoward effects of arsphenamine, of mercury, and of potassium iodide are rare. But their rarity should not exclude them from entering into our calculations.

CHAPTER XVIII.

THE SEROLOGY OF SYPHILIS.

The technic of the Wassermann test and of the various chemical tests indicative of the presence of the disease in the cerebrospinal fluid, will not be considered here as problems of syphilis. The refinements to which they have been brought are such that it seems to me that for a long time to come, at least, there will be but slow improvement over the methods of diagnosis now in use. It is the clinical facts of which they are indicative that present the problems to be discussed in this chapter.

Wassermann first demonstrated the test which bears his name in 1907. It is a modification and practical application of the Bordet-Gengou reaction which was brought out by these workers some six years before; which in turn was built up from the work of Nuttall, Buchner, Pfeiffer and Belfanti and Carbone in the phenomena of bacteriolysis and hemolysis. Although used all over the world as the diagnostic procedure *par excellence* in syphilis, the exact nature of the reaction is still unknown. Many explanations have been offered and it is possible that some of the theories advanced as to the process whereby the reaction is expressed may be correct or, at least, contain the germ of truth.

The Wassermann Reaction.—The serologic test known as the Wassermann reaction which has come into common use within the past fifteen years for the diagnosis of syphilis has marked an immense advance in our knowledge of the disease. Previous to the introduction of the Wassermann test we were compelled to depend entirely upon clinical evidences, which were, to say the least, often misleading. Hence, it can be said with truth that where once we guessed, now we know. The advantage and importance of this test and those others pertaining to the examination of the cerebrospinal fluid, is so obvious that I need say no more as to the aid they give in the diagnosis of syphilis.

Complement-fixation.—In 1901, Bordet and Gengou described what was then an extremely novel procedure for the diagnosis of infectious diseases based on the phenomenon that is known today as complement-fixation. Almost simultaneously with the announcement of Bordet and Gengou, Widal and LeSourd applied the principle of complement-fixation to the diagnosis of typhoid fever.

In 1906, Wassermann, Neisser and Bruck by a method similar to the Bordet-Gengou phenomenon announced that they could determine the presence of syphilis by means of the serum reaction of patients with this disease. The test which these workers elaborated from the original Bordet-Gengou test has come to be known throughout the world as the Wassermann reaction.

By far the great majority of serologists believe that the Wassermann reaction differs from the original Bordet-Gengou reaction in that the Bordet-Gengou reaction is a specific reaction whereas the Wassermann reaction is not. Recently, however, Wassermann has demonstrated in the blood of syphilitics a lipoid which he has succeeded in isolating and he has further shown that this substance is capable of causing the production of true antibodies. According to Wassermann, in syphilis there is an inversion of lipoid metabolism which explains why the reaction is positive, not only with extracts from the organs of a syphilitic fetus, but also with all organic extracts containing lipoid substances. Wassermann and his co-workers, Neisser and Bruck, elaborated their test only a short time after the discovery of the causative organism of syphilis had been discovered by Schaudinn and Hoffmann; and owing to lack of technical skill, which has since been overcome, they were unable at that time to grow the Treponema pallidum in pure culture. They were obliged therefore, to seek a substitute for a culture of the treponema. For this purpose they utilized an aqueous extract of the liver of a syphilitic fetus. It was not long, however, before they and others, who had almost immediately taken up the work—for its importance and the practical applications thereof were quickly realized—found that the same results could be obtained with alcoholic extracts of organs which did not contain the Treponema pallidum. These include the human heart and liver, and the heart and liver of the ox and guinea-pig. It is this fact (which Wassermann has only recently cleared up) that caused serologists to believe that a distinction existed between the phenomenon of Bordet and Gengou and the phenomenon of Wassermann.

From time to time various organic substances have been advocated as substitutes for the antigens derived from the organ extracts, including pure lipoids, cholesterin and lecithin. Sachs, in order to increase the sensitivity of the antigen, cholesterinized the same. While this procedure undoubtedly increased the delicacy of the test it has in turn caused some question as to its specificity in the minds of not a few serologists. It is not my purpose here to discuss the different technics used by different workers. It is sufficient to say that while many workers have spent much time and effort to standardize the test this has not as yet been accomplished. This is to be regretted because of its supreme importance as a diagnostic

measure for syphilis. The intricacy of the test and the various equations—personal and other—which enter into it, undoubtedly militate to a very great extent against the accuracy which should obtain, and give rise to the discordant results, which in some instances amount to deplorable errors—more frequently than is usually supposed.

Since Wassermann has, as I have just stated, explained the nature of the test, and I for one believe his explanation to be the true one, I shall not dilate here upon the various theories that have been advanced as to the nature of the test. It seems to me that to do so would serve no useful purpose. I shall therefore proceed to explain the mechanism of the Wassermann reaction in terms that can be readily understood by those not versed in the terminology and phenomena of serology. It is difficult to do this unless for the sake of brevity and clearness I omit many of the details and present only the most salient facts.

Complement.—The Wassermann reaction is based upon the following proposition. In all fresh normal serum there exists a substance known as complement which combines with any other substance when introduced into the body to form antibodies to that particular substance. The substance with which complement combines is known as antigen and hence the term "complement-fixation" because the antigen "fixes" or holds the complement.

Hemolytic and Bacteriolytic Systems.—In view of the fact that the reading of the Wassermann test depends upon the presence or absence of hemolysis, a hemolytic system is necessary as an indicator and a bacteriolytic system is necessary as a diagnostic system. The hemolytic system is made up of a suspnesion of erythrocytes which represents the antigen; an immune serum to enable the antigen and complement to combine, which is called the amboceptor; and fresh normal serum which constitutes the complement. The bacteriolytic system is composed of an extract of normal or syphilitic tissue which represents the antigen; the serum to be tested which represents the amboceptor; and fresh normal serum which represents the complement.

Technic.—Into a test-tube containing normal salt solution the serum to be tested is added; to this is added fresh normal serum obtained from the blood of some animal—usually a guinea-pig; to this is added extract of syphilitic or normal tissue. This mixture is allowed to stand in the test-tube at a temperature of 37° C. for half an hour. Then a suspension of red blood corpuscles derived from a human being or some animal is added thereto, also serum of a rabbit immunized to the blood corpuscles employed in the suspension. The mixture is now incubated again at the same temperature as before for an hour and then placed in an ice box for several

hours longer. At the end of that time the reading of the reaction is taken.

If the serum that has been tested is positive, that is if the patient has syphilis, hemolysis will not occur. If it is negative, that is if the patient has not syphilis, hemolysis will occur. The positive result is obtained because during the first incubation the complement and antigen are united and when the erythrocytes and immune serum are added later there is no complement left to unite with them and consequently hemolysis cannot occur. When the result is negative it is because the serum to be tested lacks the substance which enables the complement and antigen to unite, so that when the erythrocytes and immune serum are added later the immune serum unites with the free complement and consequently hemolysis occurs.

In taking blood from a suspected case of syphilitic infection, there are certain factors which influence the integrity of the test; and these must, therefore, always be considered whenever the test is done. One of these is the imbibing of alcohol within twenty-four hours before the blood is withdrawn. If alcohol has been taken into the blood within that time, a reaction that would otherwise be positive will be returned negative, and this negation of what should be a positive reaction may be present as long as three days after the alcohol has been taken. For this reason, a Wassermann test should not be taken until three days have elapsed after the patient has drunk any liquid containing alcohol. It is also advisable that the blood should be withdrawn while the patient's stomach is empty, as the changes which are apt to occur in the blood following a meal may cause it to hemolyze before the test can be made.

Asepsis.—It is also necessary, when blood is withdrawn for the purpose of taking a Wassermann test, that the strictest attention to aseptic details should be carried out, because, should it happen that the blood to be tested becomes contaminated with staphylococci or streptococci, a negative reaction may be returned as positive. Along with strict asepsis in withdrawing the blood, it should not be kept longer than twenty-four hours for fear of the organisms mentioned contaminating an otherwise sterile serum.

In untreated syphilis the action of the complement-fixation power of the blood is apt to be extremely variable in its reaction. That is, it may be plus today and minus tomorrow. For this reason a single negative reaction in a case of untreated syphilis is of relatively slight value in determining the presence or absence of the disease. To a lesser extent this also applies to syphilis that has been treated. It is only after repeated tests have been made, extending over a period of many months, that a patient may be considered free from syphilis if the disease is suspected in an asymptomatic form, or if the

patient is to be considered cured after treatment. The absolute determination of whether a given case is free from the disease, will be discussed further on in this chapter.

This variation in the results of the Wassermann reaction undoubtedly explains the discrepancies which so often occur when the blood of a given case is examined in different laboratories. When it is desired to check the results of a Wassermann test and the blood is sent to two or more laboratories, it is necessary that the blood for each should be drawn simultaneously and not on different days, as is often done.

It is also undoubtedly true that the results of the Wassermann reaction vary during different stages of the disease. The highest number of positive reactions are obtained in the secondary stage of the disease, while active lesions are present. The lowest number of positive results are obtained in the primary, latent, and tertiary stages, in the order named. According to Craig, whom I concede to be a most eminent authority, a positive reaction is obtained in 90 per cent of primary syphilis, *i. e.*, while the chancre is present and secondary symptoms have not yet developed. This, however, is not in accord with my own experience, which is by no means limited. I will concede that when the chancre has existed for as long as a month, that the percentage of positive reactions is very much larger than when its appearance has been noted for only a few days or a week or so. But even in this advanced stage of the evolution of the primary sore, the percentage of positive reactions is by no means as large as when the secondaries are fully developed.

In the secondary stage of syphilis it is possible that 100 per cent of untreated cases will show a positive reaction. This is the experience of Kolmer and Boas, and from personal experience I have no reason to question their results. Occasionally—very occasionally, I may say—a Wassermann taken in the secondary stage, even with active lesions present, may react negatively. It may do this once—twice, or even three times—but if the tests are repeated often enough a strongly positive Wassermann will sooner or later be obtained.

The strength of the reaction has absolutely no bearing upon the severity of the symptoms. For example, the patient's mouth may be full of mucous patches and there may be condylomata about the anus or vagina, and yet the reaction of the blood may show only one plus. Again, the patient may be in the best of health, with no symptoms whatsoever, and yet the blood examination will show four plus.

In untreated tertiary syphilis the percentage of positive Wassermann reactions will average about 95, but in cases that have been treated this percentage will be lowered to 80. In asymptomatic or latent syphilis the percentage of positive Wassermann reactions

is relatively high, and many of these cases also show a strong reaction —three or four plus. Why this should be is unknown. It is a problem of syphilis that is still unsolved. McDonagh, of London, states that a positive Wassermann, in asymptomatic syphilis, does not necessarily imply that syphilis is present, but rather that the disease has been present. With this I take decided issue, and I am in accord with Neisser and all other syphilologists that I know of, that a positive Wassermann reaction is indicative of the presence in the body of living treponemata and, therefore, that the disease still exists although it may not be active and may never become so. It can never be foretold, in a patient whose blood shows a positive Wassermann reaction, when the disease will break out. In such cases it is always a possibility that must be reckoned with, no matter how excellent may be the present state of his health.

Where syphilis has existed for many years, even if asymptomatic, it is extremely difficult to change a positive reaction into a negative one, in spite of the most vigorous and intelligent treatment. The lesions will disappear, but not the positive reaction. A certain number of these cases, if treatment is persisted in long enough, will eventually become negative, but a certain proportion will never become so and will remain positive throughout the patient's life. In these "Wassermann fast" cases, as pointed out by Fordyce, there is probably some obscure lesion that furnishes a nidus for the maintenance of the infection. It is frequently in the liver, or the central nervous system, or it may be in the spleen or heart. It has been observed, in some of these cases, that intraspinous treatment will change a positive reaction in the blood to a negative, which is a clinical fact worth remembering. A Wassermann-fast serum should cause the physician to always give a guarded prognosis as to the future. Not infrequently these patients develop syphilitic cardiovascular disease or other grave visceropathies.

Congenital Syphilis.—All infants or children, showing signs of congenital syphilis, will give a positive reaction. But this cannot be said, however, of all infants born of syphilitic mothers, as fully one-half of them give a negative reaction. Again, an infant born with a negative reaction may, after a term of years, show a positive reaction and this positive reaction, unless combated by treatment may continue to exist indefinitely. I am convinced that this form of latent congenital syphilis is the cause of the positive reaction in many individuals who deny, and with truth, ever having had any infection of which they were aware. A mother who is syphilitic, if she undergoes vigorous treatment during the period of her pregnancy, will almost certainly give birth to a healthy child with a negative reaction that will remain so permanently.

Wassermann Reaction in other Diseases.—While the Wassermann reaction is undoubtedly pathognomonic of syphilis, it is sometimes present in other disease. The Wassermann reaction shows positive in yaws, gangosa, and other trypanosomic diseases. This is to be expected when we consider the rather close relationship which these diseases bear to each other clinically and as to the causative factor. Tubercular leprosy and malaria in the febrile stage, carcinoma and sarcoma, will sometimes give a positive reaction even after syphilis has been absolutely ruled out. Following anesthesia, for a short time thereafter the blood may react positively. I do not believe that a positive reaction will be obtained in pneumonia, tuberculosis, scarlet fever or diabetes, as has been claimed by some. If such a reaction is obtained, there will undoubtedly be found an underlying syphilitic basis.

The stronger the reaction, whether symptoms are present or not, the less amenable will be the reaction to treatment. Despite the opinions of some, the reaction is more apt to become negative under the combined influence of arsphenamine and mercury than under arsphenamine alone. It is less apt, however, to change from positive to negative by the action of mercury alone, although I am convinced that it does occur. In other words, syphilis can be cured by mercury without the use of organic arsenic. I also desire to go on record as of the opinion that syphilis, in rare instances, exhausts itself without any treatment whatsoever; by which I mean that spontaneous cure can take place.

When vigorous treatment is instituted, the Wassermann reaction in the blood may change from positive to negative as early as six days following such treatment, as has been observed by Fordyce. As a rule, however, this change does not take place until from five to six weeks thereafter. In a large number of cases, unfortunately, this negative reaction sooner or later relapses to positive again. This usually happens in about four months, although it may be delayed as long as two years. In view of the fact that a positive Wassermann is absolutely indicative of syphilis, this relapse may be equally regarded as an indication that the disease is not cured and that further treatment is required. It also shows that the blood should be returned negative for at least a year, within which period repeated tests should be made, before the disease can with reasonable certainty be said to be cured.

The observations of Craig, Fordyce, and others, including myself, have shown that the sooner treatment is begun, when the disease is diagnosed, especially in the primary stage, the better will the results be in obtaining a negative reaction that will not relapse to positive. In a series of 500 cases, Craig observed the following: "In 95 primary cases 63 became negative, or 66.3 per cent; in 285 second-

ary cases, 169 or 59.3 per cent became negative; in 52 tertiary cases, 17 or 32.6 per cent became negative; and in 68 latent cases, including both early and late latent infections, 35 or 57.3 per cent became negative." In my opinion Craig's percentages of negatives in the tertiary and latent stages of the disease are rather higher than is usually found. I agree with him, however, in his opinion that the more intense the reaction, regardless of the stage of the infection, the less liable is the reaction to be influenced by treatment.

As long ago as 1910, Gennerich showed that a negative Wassermann often changed to positive following the administration of arsphenamine, the change in the reaction occurring within a few hours or as long as two weeks subsequent thereto. He called attention to the value of this phenomenon in determining whether the disease was cured or not, and also as a means of determining the presence of the syphilitic factor in certain obscure conditions in which lues was suspected as a possible cause. Similar observations were also made by Milian, Herxheimer and Michaelis.

To obtain a provocative Wassermann, arsphenamine is administered and the blood is withdrawn twelve hours after. It is withdrawn again twenty-four hours after and seventy-two hours after, at the expiration of five days, eleven days, and fourteen days, or it may be withdrawn every day for ten days.

In every instance where syphilis is suspected, even though the blood is repeatedly negative, freedom from syphilis should not be adjudged unless every specimen of blood is returned negative after a provocative injection of arsphenamine has been given. This change of a negative reaction to a positive can sometimes be obtained following an intramuscular injection of mercury, but the use of mercury is by no means as certain as when arsphenamine is used. Because of this uncertainty, I do not advise the use of mercury unless for some reason it is impossible to use arsphenamine.

Lumbar Puncture.—The advances made within recent years in our knowledge of nervous syphilis is due in a very large degree to the practice of lumbar puncture and the withdrawal of the cerebrospinal fluid for purposes of diagnosis. This route is also now used, and with at least fair success, in the combating of nervous syphilis with the specific drugs—arsphenamine and mercury.

The existence of fluid in the brain was known to the ancients, but only in pathologic cases, although Herophilus (300 B. C.) must have been aware of its existence in his many dissections of the brain and its neural appendages. No record of his observations, however, is extant. The first to give an actual description and a scientific conception of the physiologic purpose of the cerebrospinal fluid was François Magendie. In 1856 Middledorp performed a cerebral puncture on the living subject, but the first to perform spinal punc-

ture for therapeutic purposes was not Quincke, with whom lumbar puncture is usually associated, but the American, James Leonard Corning, who antedated the German by ten years.

The marked advance in our knowledge of syphilis, that has been made in the past decade and a half, has more than emphasized the importance of the facts to be learned from an examination of the spinal fluid in the diagnosis and treatment of lues. The study of

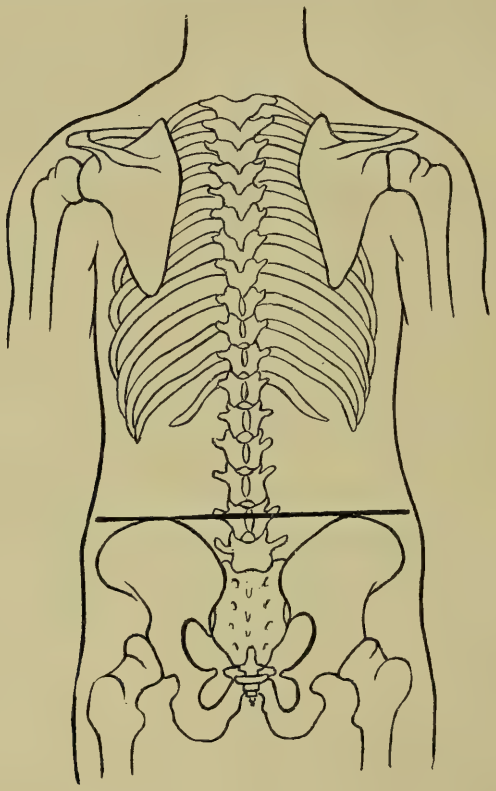


FIG. 58.—Line for lumbar puncture.

the spinal fluid has in many instances completely changed our conceptions of many diseases of the nervous system. As the Treponema pallidum has such a decided predilection for the nerve elements of the body, it is of paramount importance that this intimate and enveloping fluid of the cerebrospinal axis should be studied, and its phenomena in connection with syphillis carefully correlated, in order that we may have a complete understanding of the disease.

The dictum that every patient with syphilis should have an examination of the spinal fluid is absolute. There is ample reason for this. Dreyfus has shown that 80 per cent of syphilitics show a positive Wassermann in the spinal fluid, although many of these are asymptomatic in so far as symptoms are concerned. Fordyce whose conclusions are always of weight, in a large series of cases showed that 35 per cent of secondary syphilis showed a positive

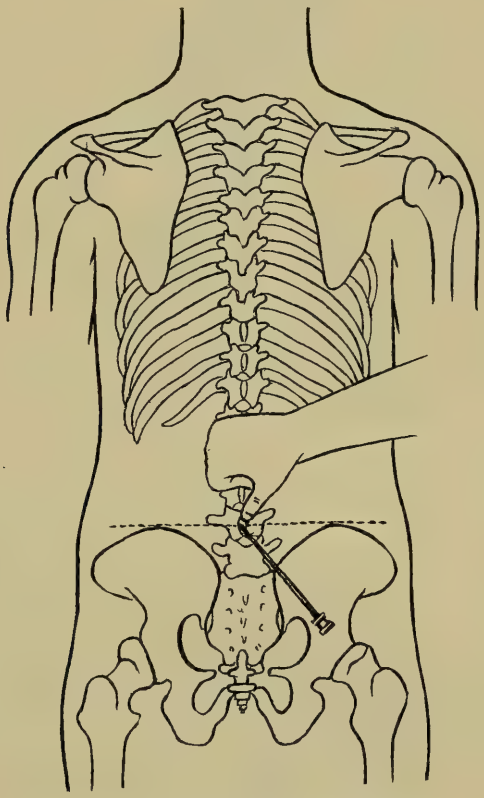


FIG. 59.—Ordinary method of inserting needle.

Wassermann in the spinal fluid. From this it can readily be inferred that every case of syphilis, in which the spinal fluid findings are positive, is a potential paretic or tabetic. I am in full accord with Fordyce, who holds that nervous syphilis really begins in the first year of the disease, although it may be many years before the lesions caused by the treponema manifest themselves as signs and symptoms of disease of the nervous system. If symptoms of involvement of the

nervous system appear, and which from their character point to syphilis as the cause, a spinal fluid Wassermann is of infinitely more value in diagnosis than a Wassermann of the blood. The blood may be, and not infrequently is, negative in nervous syphilis, but the spinal fluid never is. I make this statement advisedly because it has been and still is, often stated that in some forms of nervous syphilis —tabes for instance—the Wassermann reaction is not always positive.

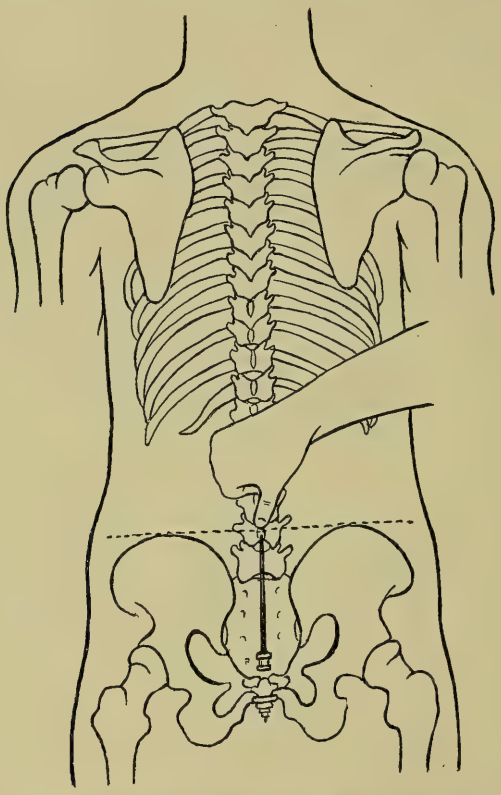


FIG. 60.—Preferred method of inserting needle.

The reason for this is because insufficient amounts of fluid are used in making the test. If fluid in sufficient amount is used, a positive reaction will almost invariably occur. In some instances in tabes the spinal fluid may be negative to the Wassermann reaction if the process is arrested or has worn itself out, as it were. These cases may be far advanced in the disease from a clinical standpoint; but this simply means that the damage has been done.

The findings in the spinal fluid allow not only a diagnosis of

syphilis to be made, but a proper understanding of these findings will enable the physician in most instances to differentiate between

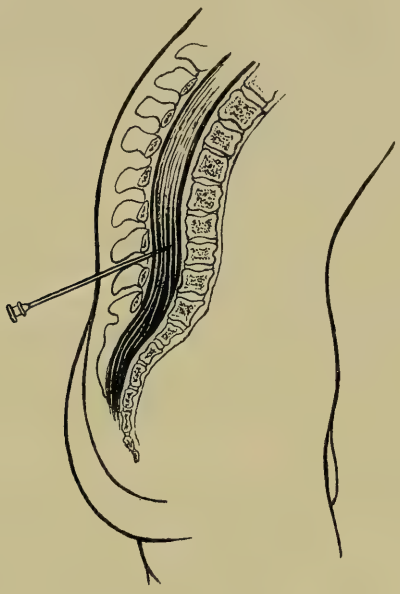


FIG. 61.—Vertical section of spinal region showing position of needle in cauda equina.

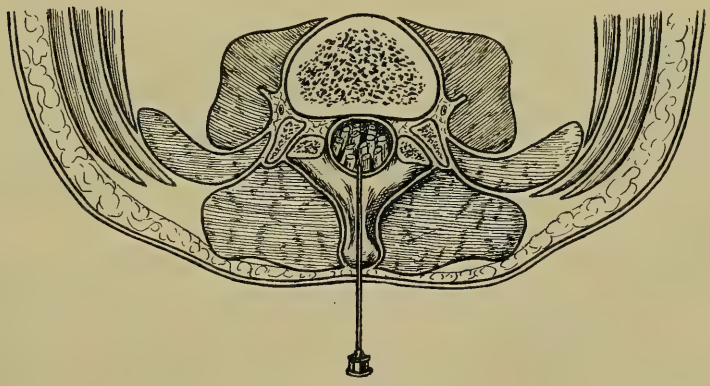


FIG. 62.—Transverse section of spinal region showing needle in the cauda equina.

the different forms of nervous syphilis, which is most important in so far as prognosis is concerned, for the treatment is practically the same in all cases.

As I have already stated, the Wassermann test will show involvement of the nervous system before any symptoms whatsoever are present. During the first year of the disease this involvement, although often present, is not infrequently transitory and in many instances spontaneous cure is undoubtedly effected, otherwise there would be many more cases of nervous syphilis than there are. Later, however, in the course of the disease, which means that the positive Wassermann noted so frequently in the secondary stage has continued to persist, the presence of a positive Wassermann in the spinal fluid is of far graver significance. It then absolutely indicates, whether symptoms are present or not, that the disease has invaded the nervous axis and prompt and vigorous treatment is imperatively called for, if we are to save the patient from the terrors of paresis, tabes, or cerebral syphilis.

Recently Lotmar has offered convincing evidence that the spinal fluid is sometimes Wassermann positive in tumors of the brain or spinal cord. He is of the opinion that this change in the fluid is due to the presence of lipoids. I see no reason to deny his statement and therefore I accept it.

In the syphilitic psychosis known as paresis or general paralysis of the insane (G. P. I.), there is invariably a positive Wassermann, even in as small an amount of fluid as 0.1 cc. There is also a positive reaction in the blood, and the presence of these two reactions is pathognomonic of paresis. All other tests are corroborative and nothing more. In these two respects, therefore, much aid is offered in the differential diagnosis between paresis and cerebral syphilis, diseases which in many instances it is impossible to distinguish clinically. In cerebral syphilis, although it has been stated to the contrary, there is invariably a positive Wassermann in the spinal fluid, but it is always in larger amount than in paresis. Also in cerebral syphilis in about 10 to 15 per cent of cases the blood may be negative. This never occurs in paresis. In paresis, as in tabes, at the terminal stage the spinal fluid may be negative. This is simply indicative that the pathologic process is complete and, as in tabes, the damage has been done.

In tabes, if 1 cc of fluid is tested, the Wassermann reaction will be found to be positive in nearly 100 per cent. If a smaller amount is tested, for example, 0.2 cc, only about 10 per cent will be found to be positive. This undoubtedly explains why it is often asserted that from 40 to 50 per cent of tabetics show a negative Wassermann in the spinal fluid. If the Wassermann is negative in this small amount of fluid, and if symptoms are present, it indicates that the disease is either arrested from some spontaneous cause or that it has been cured by therapeutic measures, if such have been given

intelligently. In tabes the blood is positive in approximately 75 per cent of cases.

Briefly as I have stated them these are the absolute findings in so far as the Wassermann reaction is concerned in all forms of nervous syphilis. But aside from the Wassermann test, there are certain other chemical tests and the computation of the cellular elements found in the spinal fluid, that are of extreme value as corroborative evidence in the diagnosis of syphilis of the nervous system. They are not, however, as is the Wassermann, specific tests since they frequently occur in nervous diseases due to causes other than syphilis.

In order to obtain more precise readings of positive Wassermann reactions Vernes devised a colorimetric scale of tints ranging from 0 to 8. He sought to establish a more closely accurate method for comparing hemolytic results. The method is logical and valuable in that it allows of a closer scrutiny of the degree of infection and of the result of treatment. Its use in this country seems to be limited to only a comparatively few workers, although in Europe it has has been extensively employed since it was first described by its originator in 1910.

A test which some serologists seem to think may eventually supplant the Wassermann test is that originated in 1918 by Sachs and Georgi and known as the Sachs-Georgi test. It is a flocculation test due to a physico-chemical reaction between seroglobulins and lipoid extract. Hemolysis does not enter into the mechanism of the Sachs-Georgi reaction as only one biologic reagent—antigen—is used. It is asserted by not a few serologists that with this test non-specific reactions are less frequent than with the Wassermann test. It is also said to be positive earlier and to remain so longer than the Wassermann test. It parallels the Wassermann test in from 85 to 90 per cent. It is too soon perhaps to say that it will supplant the Wassermann test for syphilis. If it stands the test of time it is quite possible, however, that it will do so because of its more simplified technic.

From time to time various workers have put forth tests which they believed would supplant the Wassermann because of simplified technic. None of them have as yet stood the test of time. Of these newer and simpler tests the formaldehyde-gel test of Gates and Papacostas seems to have the greatest possibilities.

Lange's Colloidal-gold Test.—A test, which is considered important by some, is the Lange colloidal-gold test. The exact nature of the reaction in this test is not known. It occurs when the protein content of the fluid is increased, but it cannot be said that it is due to this increase. It is in all probability a physical reaction of an electrolytic nature rather than an immunity reac-

tion as held by some. The test is positive in 95 per cent of all cases of paresis and when present with a positive Wassermann of 0.1 cc of fluid a diagnosis of paresis can be made without hesitation. Alone, however, it is not specific as the so-called "paretic curve" may be present in organic nervous disease not due to syphilis; notably, meningitis, poliomyelitis and multiple sclerosis. In cerebral syphilis and in tabes the "paretic curve" is not encountered, but instead the test shows when positive as the "luetic curve," which differs from the paretic curve in that the numbers by which the curve is expressed are not as high. Kyrle, Brandt and Mras however, from results obtained in an extensive series, believe that the reaction of the spinal fluid to colloidal gold is the first evidence of a pathologic state in the central nervous system. They also believe that its persistence is of prognostic import in that in such cases relapse or a grave form of nervous involvement is presaged.

Personally I have come to disregard the colloidal-gold test as being entirely too aberrant for accurate diagnosis.

Globulin Increase.—A much more reliable confirmatory test in my opinion than the gold test is the test for globulin increase. In all syphilitic diseases of the nervous system, and also in some nervous diseases which are not syphilitic, the protein content of the spinal fluid is invariably increased. Tests to detect the globulin contained therein have therefore been devised. The tests most frequently used are the Nonne-Apelt, the Noguchi and the Pandy. If syphilis of the nervous system is present the globulin will be found to be increased. So constant is this increase that were it not also present in other nervous diseases I would consider it pathognomonic of syphilitic nervous disease. Although most valuable as confirmative evidence the test is not, therefore, specific for luetic disease.

Cellular Element.—An important factor in the diagnosis and prognosis of syphilitic nervous disease is the computation of the cellular elements contained in the spinal fluid. When these elements are increased in number they indicate an inflammatory reaction existing in the leptomeninges. This inflammatory reaction, however, may not necessarily be syphilitic, and to that extent the value of the count is diminished as a diagnostic feature of syphilis. A high count indicates an acute process, and if the condition is syphilitic it is (other things being considered), of favorable prognostic import, as acute syphilitic processes are more amenable to treatment than those which are chronic or which have passed into the degenerative stage when the cell count will be low. As an indicator, therefore, of an acute or chronic process and within these bounds the cell count is most valuable.

The highest cell count is to be found in syphilitic meningitis, when

the number of cells may be increased from six to ten, which is the normal number, to as high as a thousand or more to the c.mm. In paresis the cell count is not high, rarely over a hundred and it may be as low as twenty. The same is true of cerebral syphilis where, however, as just stated, the higher the count the more favorable will be the prognosis as compared with a count that is low. In tabes the count will be high if the process is running an acute course. It will be low if the degenerative process is complete. For that reason, treatment is practically valueless in tabes where the cell count is low.

When the cell count in any syphilitic nervous disease is hyperlymphocytic, or increased far above the normal number of cells, it indicates an active form of meningeal irritation, an exudative process, as it were, and therefore a recent one. These cases are those which are most amenable to treatment and offer the best prognosis as to arrest or possible cure. But those cases, in which the cell count is low and approaches most nearly the normal, indicate that the active exudative process is past and the disease is either in abeyance or else that the harm done is beyond cure. These cases should not receive intraspinous treatment, or if given, the prognosis as to the results possible to achieve should be most guarded. Cases also which, in spite of the most energetic treatment, still show a positive Wassermann reaction, should also be given a guarded prognosis in so far as relapse is concerned even when they appear to have been benefited clinically by the treatment. I may add that in paresis the Wassermann is never changed to negative, and this fact is a valuable aid in diagnosing this psychosis from others of a syphilitic nature.

From the facts as stated here it can be seen that in conjunction with the clinical signs of the disease a diagnosis of the various forms of nervous syphilis can be made, and also to a more limited extent their course and probability of cure can be prognosticated.

CHAPTER XIX.

THE WASSERMANN REACTION IN DISEASES OTHER THAN SYPHILIS.

When Wassermann, Neisser and Bruck first applied the serological test which bears the name of the first of these three workers, they believed it to be a specific antigen-antibody reaction. Although in its practical application the Wassermann reaction is undoubtedly specific for syphilis, this is so only in its narrowest meaning, that is only when antigens prepared from pure cultures of the Treponema pallidum are used. But because it is not specific is the reason why perhaps, it reacts with the precision that we know it does. For, if we compare the results of complement-fixation obtained in other diseases the same unvarying exactitude is by no means so frequent.

Since we know that the mechanism of the reaction may not represent a true specific reaction, it is possible that it may occur in other conditions than syphilis. Within certain limits we know this to be true, and it will be my purpose in this chapter to inquire into and define those deviations, especially as they affect the diagnosis of syphilis for which the Wassermann reaction is the diagnostic test *par excellence.*

Scarlet Fever.—Shortly after the Wassermann reaction came into general use for the diagnosis of syphilis, Much and Eichelberg of Hamburg (1908) reported that in 25 cases of scarlet fever the blood reacted positively in 10. A year later Much reported another series of 100 cases in which the reaction was positive in 45. From 0.3 to 0.4 cc of serum was used which was considerably in excess of the 0.2 cc originally recommended by Wassermann. Working simultaneously, Bruck and Cohn in 28 cases of scarlet fever in which the blood was taken when the disease was at its height obtained 8 positive results. They observed however, that the sera of their patients did not react positively with all of the extracts used, reacting to one and failing to react to another and *vice versa;* whereas the sera of the syphilitics used as controls reacted positively in every instance with all of the extracts. Following these reports Boas and Hague adhering strictly to Wassermann's original technic tested the sera of 61 scarlet fever patients in all stages of the disease. Of these, 1 only—a girl, aged nine years with no evidences

of congenital or acquired syphilis —gave a positive reaction, which two weeks later changed to negative.

Tuberculosis.—Weil and Braun, Elias, Neubauer, Porges and Salomon in 1908 reported that the Wassermann reaction was sometimes positive in tuberculosis. In 21 cases of phthisis pulmonalis Weil and Braun obtained 2 positive reactions. Elias, Neubauer, Porges and Salomon, in 25 cases reported collectively found 5 positive reactions. All of these observers qualified their observations by stating that none of these positive reactions were typical when compared with the reactions with syphilitic sera. In a series of 49 cases of tuberculous disease involving different parts of the body Boas obtained 3 positive reactions, and in these 3 he admits that syphilis was undoubtedly present in a latent or asymptomatic form. Practically therefore, all of the reactions were negative. In 1912 Marchildon published the results of his tests in a series of tuberculous patients. Two of them who went to necropsy reacted positively. A third who had been diagnosed as having a tuberculous bone lesion gave a positive reaction, and later the diagnosis was changed to syphilitic bone disease and the lesions cleared up under antisyphilitic treatment. This case must therefore be excluded.

Typhoid.—Weil and Braun tested the sera of 20 typhoid patients and obtained 3 positive reactions. Only negative reactions were obtained by Bauer and Meier in 26 cases. Similar results have been obtained by numerous other observers.

Malaria.—It has been claimed by some that the blood of a patient with malaria gives a positive reaction. These claims which have been advanced from time to time do not, upon investigation, appear to be very convincing. Craig has observed that in the febrile stage of this disease an occasional positive reaction is obtained. Thompson has also recorded similar occurrences. With the disappearance of the fever and the plasmodia the reaction returns to negative.

Jaundice.—A number of observers have investigated the influence of icterus on the Wassermann reaction. Scherdemandel asserts that the serum of a patient with jaundice cannot be used in making the test because of the presence of bile. Bar and Dauney are of the opinion that when icterus is present a positive reaction is inevitable and because of this fact a positive reaction in a new-born infant with icterus neonatorum does not necessarily imply syphilis. These statements do not always hold however, since it has been noted that while the sera of icteric infants does not hemolyze as rapidly as the sera of non-icteric infants yet hemolysis does take place although much delayed. In acquired syphilis icterus is by no means uncommon, especially in the early secondary stage when the blood reaction is almost invariably positive; while icterus neonatorum is extremely

frequent from perfectly natural causes in non-syphilitic infants, it is comparatively rarely encountered in congenital syphilis despite the fact that the liver is the organ most frequently attacked, and at necropsy of infants born dead or dying shortly after birth from congenital syphilis is found to be literally swarming with trepone-mata.

Chronic Plumbism.—Positive Wassermann reactions have been reported in patients suffering with chronic plumbism. Since none of the cases examined showed any evidences of syphilis, past or present, Dreyer and Schmitter, who made the report, concluded—very illogically in my opinion—that chronic lead poisoning occasion-ally caused a positive Wassermann reaction. The effect of plum-bism on the Wassermann reaction was later investigated by Perussia who tested the sera of artificially poisoned rabbits. His results were uniformly negative.

Pseudoleukemia.—It has been observed that a positive reaction is sometimes present in pseudoleukemia—Hodgkin's disease. Caan has reported 4 cases. Other investigators however have not con-firmed his findings. In other hematopoietic diseases and in sepsis and variola, Xylander obtained only negative reactions; although it must be mentioned that Massaglia and Barganti in a patient with severe pernicious anemia obtained a positive reaction. Others again, obtained negative results. Positive reactions have been known to occur in acute yellow atrophy of the liver. Lochlein reported 2 cases in 1910. Numerous observers have reported positive reactions in diabetes. It has also been observed in acidosis. In 5 cases of eclampsia, during and subsequent to the attacks, Gross and Bunzel found positive reactions, but fourteen days later all of these cases reacted negatively. In a series of 7 cases in which the blood was taken during and shortly after the convulsions Boas obtained only negative reactions.

Vincent's Angina.—Much reported a case of Vincent's angina which reacted positively and Sobernheim offset this by reporting a case which reacted negatively. The serological tests in this disease taken by Boas all reacted negatively.

Lobar Pneumonia.—Weil and Braun have reported positive reac-tions in lobar pneumonia. Others I believe have reported the same but after careful search through the literature I have been unable to find any further reports except those mentioned.

Thyrogenous Psychosis.—Riggs has recently called attention to the large number of positive reactions obtained by him in a series of cases which had been diagnosed as "thyrogenous psychosis." These patients were all insane with two exceptions. In most of them there was exophthalmos and tachycardia. The mental symptoms included delusions and irritability that sometimes

developed into maniacal excitement; others again showed a negative phase characterized by slowness of speech, mental lassitude and indifference to surroundings. None displayed homicidal or suicidal tendencies. The prevailing mental tone was fear and apprehension.

Nervous Diseases.—The Wassermann reaction has been found to be positive in dementia præcox, also in epilepsy and multiple sclerosis—although this last is, strange to say, rarely if ever caused by syphilis.

Leprosy.—A number of observers have reported positive Wassermann reactions in leprosy—especially the tubercular form; whereas in the anesthetic type of this disease a positive reaction was only rarely encountered.

Frambœsia.—It has been established that the Wassermann reaction is positive in frambœsia or yaws.

Gangosa.—It is also sometimes positive in gangosa, a disease indigenous to Polynesia and tropical Africa and South America.

Spirochætes.—As to the other spirochetal diseases such as Leishmaniasis—kala-azar or espundia, verruga peruviana, Oroya or Carrion's disease, relapsing fever, sodoku or rat bite fever, cat bite fever, I am unable to say whether they give a positive reaction or not. Reasoning from analogy I would infer they do.

Malignant Growths.—The Wassermann reaction has frequently been observed to be positive in malignant growths. In 4 out of 14 cases of malignancy, Weil and Braun obtained a positive reaction. Elias, Neubauer, Porges and Salomon, Simon, Schenck and others have reported similar instances. Newmark reported positive reactions in 2 cases of neural tumor. One was that of a woman, aged fifty-three years, in which a diagnosis of tumor cerebri had been made. She also had a small carcinoma of the breast. The Wassermann was positive in the blood and in the spinal fluid. Necropsy showed that she had a gliosarcoma. The second was also a woman, aged forty-five years, in whom the blood and spinal fluid gave a positive reaction. An intradural psammoma was removed surgically. The observation of these facts caused Newmark to ask: "Does the triad of carcinoma, sarcoma and a positive Wassermann signify anything more than fortuitious concourse of two kinds of malignant growth and syphilis? Or is there a causative relation between the tumors or between one or the other of the tumors and the Wassermann reaction?" Czerny and Caan, in the Heidelberg Cancer Institute, took a Wassermann of all cancer patients admitted thereto and were surprised to note the frequency of positive reactions. The concomitance of a positive Wassermann reaction with a fibroma located in the cerebello-pontile angle has been reported by Oppenheim, and a similar instance has also been reported by Marburg. In neither of these cases was there a history

of syphilis, but there was more or less temporary improvement under antisyphilitic treatment. Foerster observed a patient with a positive Wassermann reaction from whom a spinal endothelioma was removed. This patient later developed a hemiopsia which, I might add in passing, is almost invariably caused by syphilis.

In a series of 215 tumors of various kinds, including carcinoma, sarcoma and epithelioma, reported by Fox, the Wassermann reaction was negative in all but 5. Of these, 3 admitted syphilitic infection and the other 2 were uncertain.

Some seven years ago, Newlin presented a series of 43 patients in whom syphilis was apparently non-existent but showing positive reactions. While realizing the ubiquity of the disease he confessed that his findings came to him somewhat as a shock. For example, a case of Henoch's purpura in a woman, aged fifty years, and as far as could be humanly said, of blameless life and with no signs of syphilis either acquired or congenital. Twenty years before she was supposed to have had phthisis. Three years before the Wassermann was taken she had slight attacks of hemoptysis, and her case had been diagnosed as one of pulmonary tuberculosis. Later because of abdominal pain and hemorrhage from the rectum a diagnosis of duodenal ulcer had been made. When she came to Newlin she was extremely neurasthenic, with reduced vision but showing no ocular lesions except a slight vitreous haze. A diagnosis of Henoch's purpura was made because of the presence of purpuric spots varying in size from a one cent piece to a half dollar. Examination of her brother's blood was negative and his skin reaction to the Noguchi luetin test was also negative. Another patient had been diagnosed as having incipient tuberculosis. Syphilis was absolutely denied. Two injections of arsphenamine restored him to health. In 14 of the series epilepsy was present; others had neurasthenia, habit spasm, chorea, arteriosclerosis. All were given antisyphilitic treatment and a number showed marked improvement therefrom.

It is undoubtedly true that the Wassermann reaction may be negative and yet syphilis is present. This occurs not infrequently where there are untreated lesions of the skin and mucous membranes in the tertiary stage. Reyn was the first, to my knowledge, to call attention to this phenomenon, and his opinion is that the extent of the cutaneous and mucous lesions and their duration are factors that influence the reaction. Foerster has also called attention to similar phenomena. I might add in connection with this that, although it is not so well known, the Wassermann reaction is frequently negative in precocious malignant syphilis.

There are certain other factors not pathologic which are accused of more or less influencing the reaction. It is most important to

know them as a lack of knowledge in this respect may render a test nugatory, perhaps very much to the patient's detriment.

Anesthesia.—It is somewhat extensively believed, that anesthesia influences the Wassermann reaction, in that ether or chloroform narcosis—especially the latter may cause a positive reaction to occur in a serum that is negative. As long ago as 1910 Wolfsohn reported that immediately following anesthesia if the serum was examined it would show a positive reaction, and the longer the anesthesia had been the more pronounced would be the reaction, and this condition of positiveness would continue for several days thereafter. A similar report was made by Reicher. Some two years later Cherry inquired into this phenomenon at considerable length. He could find no evidence to confirm the reports of these continental writers. Boas examined 30 persons in various stages of anesthesia and found the reaction negative in every instance. McDonagh asserts that anesthesia tends to cause a negative reaction to show positive and that anesthesia prevents the action of complement. The following is the opinion of Craig: "In surgical practice weak positive reactions are sometimes noted in blood sera collected shortly after ether and chloroform anesthesia, so that the test should not be made upon patients who have been anesthetized until at least two days have elapsed since the anesthetic was administered."

Alcohol.—In 1911 Nichols and Craig called attention to the fact that the ingestion of alcohol would sometimes convert a strongly positive reaction into a negative and that this negativeness might continue as long as three days. Others, including myself, have observed this although Boas in his monograph would seem to challenge it; but I am convinced that alcohol has this effect and therefore it is of the utmost importance from the practical standpoint to inquire strictly into whether the patient has indulged in alcoholic liquors within twenty-four hours before the blood is taken. I am in accord with Craig who believes that alcohol renders inert the substance in the blood serum which reacts with the lipoids in the antigen extracts and thus causes an otherwise positive serum to react negatively. It is possible that ether and chloroform anesthesia act in a somewhat similar though opposite manner by their reaction on the hepatic cells causing an excess of lipoids and thus giving rise to a positive reaction in a serum that would otherwise be negative.

Asepsis.—Another fact of very great importance is that certain bacteria such as the staphylococci and the streptococci should they by any chance contaminate the serum to be tested will invalidate the test by creating a positive reaction in an otherwise normal serum. For that reason it is absolutely necessary that when blood is withdrawn for the purpose of taking a Wassermann reaction the most careful attention to aseptic details should be carried out, and the

blood to be tested should be examined as soon thereafter as possible. Unless this is done it can be readily appreciated how unfortunate mistakes can occur.

Blood for taking a Wassermann reaction should not be withdrawn immediately after a meal. It almost invariably hemolyzes and thus necessitates repeating the procedure, to which the patient not infrequently objects.

Cadaveric Blood.—It has been stated by McDonagh, Bisgard and others that blood withdrawn from a patient who is dying, and also blood withdrawn shortly after death—cadaveric blood—is frequently positive. The more recent researches of Moody, Jackson and LeCount would seem to contradict this. Their findings are that if the blood is withdrawn later than twelve hours after death the test is unreliable. If taken immediately after death or before post-mortem changes have set in the test will react positively if syphilis is present and negatively if not. The only exception to be noted is that in patients dying with some acute infection the reaction is often positive although syphilis was not present. Still more recently Stuart Graves has confirmed these findings in a series of necropsies covering a period of nearly six years. While it seems to me that this is of academic rather than of practical interest yet it can be of import from a medico-legal point of view.

Summary.—I shall now briefly summarize my conclusions from the facts as they appear to me.

Scarlet Fever.—That the Wassermann reaction is ever positive in the sera of scarlet fever patients unless syphilis is present I do not believe. It will be observed that most of these positive reactions noted in scarlet fever and, I may add, in other diseases as well, were reported when the reaction was a comparatively recent addition to diagnostic serology. Improvement in the technic of making the test has so sharpened its accuracy that these former errors of interpretation no longer occur. If a strongly positive reaction is present in scarlet fever it is not due to this exanthem but to syphilis.

Tuberculosis.—As to the Wassermann reaction being positive in tuberculosis, either of the lungs or of the bones, skin, intestines or other organs. there is absolutely no reason to assume this from the data before us. Syphilis undoubtedly complicates tuberculosis. In certain lesions of the bones, the testicles in men and the external genitals in women, and in certain skin lesions, notably lupus erythematosus, differential diagnosis between the two diseases is sometimes clinically difficult. I am also inclined to believe that quite a number of cases of so-called fibroid phthisis are syphilitic rather than tuberculous. Tuberculosis unless complicated with syphilis never gives a positive Wassermann reaction.

Typhoid.—There is no reason to believe that typhoid fever in any way influences the Wassermann reaction. The presence of a positive reaction during the course of this disease is indicative only of syphilis.

Malaria.—In malaria I am inclined to accept Craig and Thompson's statements that in rare instances during the active or febrile stage of this infection the blood reacts positively.

Jaundice.—There is no proof in my opinion that the presence of bile in the blood influences the Wassermann reaction in any way whatsoever. Personally I have never known the serum of a patient with syphilitic icterus to give other than a positive reaction.

Plumbism.—The influence of plumbism upon the Wassermann reaction may be regarded as absolutely negligible.

Pseudoleukemia.—The presence of a positive reaction in pseudoleukemia—Hodgkin's disease is possible and probable. The same is true of pernicious anemia and other hematopoietic diseases; it is also true of acute yellow atrophy of the liver and diabetes. The reason for this is not hard to find, because all of these diseases frequently rest upon a syphilitic basis. Especially is this true of diabetes, which, in a larger percentage than is usually supposed is due to either a gummatous pachymeningitis of the floor of the fourth ventricle or to gummatous disease of the pancreas.

Eclampsia.—While eclampsia is more frequent in syphilitic women than in those free from the disease yet to my mind the evidence is totally inadequate as to this condition reversing the reaction either one way or the other.

Vincent's Angina.—There is no connection between Vincent's angina and syphilis although both are spirochetal diseases. If the Wassermann reaction is positive in this form of sore throat it is due to syphilis.

Lobar Pneumonia.—As to the Wassermann reaction being positive in some cases of lobar pneumonia it can be dismissed by saying that a positive reaction coincident with this disease can only mean that syphilis is also present.

Thyrogenous Psychosis.—The cases of "thyrogenous psychosis" mentioned by Riggs, by which I infer he means a psychosis grafted on Basedow's syndrome, can undoubtedly be caused by syphilis and therefore a positive Wassermann reaction would be a natural concomitant. Thompson and others have reported syphilis of the thyroid with the pathognomonic signs of exophthalmos and tachycardia which accompany involvement of this gland. The very recent researches of Pentagna in endocrine dysfunction have gone far to prove the overwhelming influence of syphilis in causing these conditions.

Nervous Diseases.—It cannot be denied that the Wassermann reaction may be positive in dementia præcox; for there is absolutely no reason why a patient suffering with this psychosis cannot acquire syphilis. Syphilitic psychoses as a rule do not manifest themselves in this form of mental aberrancy but there is nothing to prevent them from so doing. In so far as dementia præcox is concerned I agree with Tarnowsky that in many instances it represents a terminal dystrophy, three or four generations removed from a syphilitic progenitor.

A positive Wassermann is not infrequently noted in epilepsy, multiple sclerosis and tumor cerebri. There is no reason why this should not be when these conditions are caused by syphilis. When they are not so caused the Wassermann reaction is absent.

Leprosy.—I believe the Wassermann reaction is sometimes—although rarely—positive in tubercular leprosy. But in this connection I desire to call the reader's attention to the fact that leprosy, as many observers have noted, is frequently complicated with syphilis. It is possible therefore that in some instances the positive reaction is due to an unrecognized syphilitic infection.

Frambœsia.—The presence of a positive Wassermann reaction in frambœsia or yaws and also at times in gangosa I can readily understand. I hold with Hutchinson that syphilis and frambœsia were originally one disease but the influence of time and place have separated them into the two more or less closely related pathologic entities that they now are.

Malignant Growths.—A positive Wassermann in a patient suffering with malignant disease is by no means uncommon. In many instances I believe there is a relationship existing between the two dyscrasias. Syphilis, I am firmly convinced is often the starting point of cancer. I have elsewhere stated my views on this subject.[1]

The series of cases reported by Newlin in which syphilis was apparently not present although showing a positive Wassermann reaction, are not to my mind difficult to explain. They all had syphilis and their different maladies were but different expressions of the same disease. It is quite possible that many of these patients may have acquired the disease innocently or as "syphilis d' emblée" and consequently were unaware of the infection. In some it might have been delayed hereditary syphilis. As pointed out by Fournier and Oppenheim, delayed hereditary syphilis sometimes does not appear until the third or fourth decade of life. Again, as every syphilologist knows, the patient while admitting the risk will deny — and in good faith—that he ever had the disease, because he never had a chancre or any of the ordinary signs of the disease. All this

[1] Syphilis and Malignancy. The American Journal of Syphilis, St. Louis, Mo., vol. ii, No. 1.

is possible because the chancre may never have been recognized and the secondary roseola may have been so slight and ephemeral as to have passed unnoticed. The secondary stage of the disease may have been skipped—this not infrequently happens. Occult syphilis—unrecognized syphilis—is a fact that cannot be denied. That syphilis is a factor—a most important factor—in causing diseases which on their face are not so regarded is held by all advanced clinicians. In this connection I would advise the reader to study Lewellys F. Barker's masterly monograph, "The Importance of a Knowledge of Syphilis, and Especially of Visceral Syphilis for General Medical Diagnosis."

The phenomenon of the Wassermann reaction can undoubtedly be influenced in various ways so that its reading does not register truly. But these deviations can all be accounted for so that an accurate diagnostic conclusion can be reached. In most of the positive reactions here recorded as occurring in diseases other than syphilis they have almost invariably been weakly positive. It is the consensus of opinion among serologists and syphilologists as well that a weakly positive Wassermann reaction is of value only when the serum is that of a patient who has been treated for syphilis. In the absence of definite signs or symptoms of the disease or in the presence of puzzling or undefinable phenomena a weakly positive reaction is of no significance whatsoever. The specific reactions obtained in non-syphilitic diseases are of this character. They have been observed most frequently in obscure nervous disorders associated with motor unrest or a spasmodic tendency such as tics, fainting spells and convulsions. The sera of these cases are most apt to be positive with a non-cholesterinized antigen, but why it should be so is unexplainable.

Even in the presence of syphilis the Wassermann reaction may be positive today and negative tomorrow. The reason for these changes from day to day in some sera we do not know. We only know that they occur. It is an element of uncertainty that must at times enter into the diagnosis.

The same is true of the positive Wassermann reaction produced by a provocative injection of arsphenamine. We are still in the dark as to its exact nature. There are those who believe it to be anaphylactic and others who contend that it is quite different. I shall not pass upon it. But of this I am certain, a positive Wassermann reaction is indicative of syphilis and nothing else. No matter what else may be added thereto, the person who has it has syphilis. It is the one test in medicine that is exact, that is absolute, and that cannot be denied.

CHAPTER XX.

REINFECTION AND SUPERINFECTION IN SYPHILIS.

The possibility of more than one infection with syphilis, that is, the acquirement of the disease a second time, has been much discussed, particularly since the advent of arsphenamine.

It was formerly supposed that reinfection was rare, indeed, some syphilologists went so far as to deny it altogether. With the treatment now in vogue it is possible that these views are subject to modification. The protean aspect of syphilitic lesions has always rendered their recognition from a clinical standpoint alone—and that was all the older observers had to go by—in many instances extremely difficult and open to question. For that reason cases reported by some of the older writers undoubtedly, in some instances, represented recrudescences rather than reinfections. Within the last few years, however, there has appeared in the literature a number of apparently well authenticated cases of a second and then of a third and fourth infection. Many of these cases have been most closely scrutinized both parasitologically and serologically as well as from the clinical standpoint by very competent observers. As is discussed in the chapter on the Serology of Syphilis, to absolutely determine when a cure is final and complete is extremely difficult; and in some of these cases presented there is still the possibility of a recrudescence of a previous infection; rather than a reinfection. The weak link in the chain of evidence in many of the reports, is the comparatively short time that has elapsed between the first and second infections. But it cannot be gainsaid that the repeated occurrence of such cases in which the literature now abounds goes far to prove that the present methods of treatment are capable, in some instances at least, of entirely eradicating the disease. Such being the case reinfection may be regarded as an encouraging evidence of the efficiency of proper treatment.

As I have already stated, the older writers were very skeptical as to reinfection. Ricord believed in permanent immunity after a single infection; so did the elder Fournier. However, from time to time reports of a second infection appeared and Felix John succeeded in collecting 356 such reports. In his collection John applied the most exacting criteria and he found that in 14 instances, at least, every possible objection was met. In these 14 cases the

first infection was in every instance diagnosed as syphilis by men above the average in clinical skill and experience; secondary and tertiary manifestations followed the primary lesion and many years later another lesion was acquired and again the disease ran its usual, though somewhat milder, course. Sixteen other cases in his series are to my mind just as convincing in so far as internal evidence of a second infection is concerned. Many of the other cases offer strongly corroborative evidence of the possibility of reinfection. Altogether John's interesting and painstaking monograph shows that reinfection with syphilis is possible.

In order to establish the fact of a reinfection with syphilis, it is necessary for two distinct attacks of primary and secondary syphilis to have been observed in the same patient and by the same observer if possible. Hutchinson relates 2 cases, in 1 of which the patient passed through two attacks of primary and secondary syphilis at an interval of five years; in the other the patient is said to have had three attacks at intervals of fourteen and nine years. Berkley Hill reported the case of a surgeon who acquired the disease in the usual way; eleven years later he contracted a digital chancre which was followed by symptoms of secondary syphilis.

Be this as it may, it is undoubtedly true that many cases of so-called secondary infection are not true reinfection but recrudescent lesions resembling more or less a primary sore and which are by no means uncommon in tertiary syphilis. There are three forms of recrudescent syphilis which are apt to convey the impression of a second infection, but which, if carefully analyzed, can almost invariably be differentiated from a new infection. These are chancre redux, chancriform gumma and recurrent roseola. The chancre redux, or relapsing chancre, partakes of all of the characteristics of a primary chancre except that there is no glandular induration in the vicinity of the lesion as there would be if the sore was primary. Another most important element in the diagnosis is the Wassermann reaction. If the sore is primary, the Wassermann will in all probability be negative, but if it is a chancre redux it is almost certain to be positive. The chancre redux develops on the site of the primary sore and may appear at any time from a month to more than a quarter of a century, as I have seen, after the appearance of the initial lesion. The chancriform gumma in many instances very closely resembles a primary sore, but it lacks the induration which characterizes the true chancre; there is also no adenopathy, and the Wassermann is positive. Recurrent roseola is rare but it undoubtedly occurs, usually in the later secondary period. It is much more permanent than that following a primary infection and the eruptive areas as a rule are considerably larger and more annular in outline. In the study of the supposed cases of reinfection the possibility of

superinfection must always be considered, that is, a primary sore imposed upon an already existing syphilis. While this phenomenon is very rare, it yet undoubtedly occurs and still further confuses the diagnosis. Mentberger in commenting upon the report of Felix John is of the opinion that only 119 of the 356 cases described by him as reinfections fulfill the necessary conditions which would warrant their being described as reinfections.

Besides the three just enumerated there are other sources of error in diagnosing a second infection of syphilis. Among these are the general eruption which sometimes, although rarely, accompanies or follows a chancroid. Impetigo contagiosa, ecthyma, or some one of the multitudinous forms of eczema have been, and often are for that matter, mistaken for syphilis, and if any of these follow a genuine attack of the disease they may be cited as a second infection. This possibility is greatly increased if by any chance they have been preceded by a chancre redux. Or again, the first attack may have been any one of these skin lesions, and the second a true syphilitic eruption. Occasionally a chancroid or mucous patch may become indurated and thus be mistaken for a chancre, but in such an instance there will be no secondary eruption and if the lesion is a chancroid there will almost invariably follow a suppurating bubo which is a most rare occurrence as a concomitant of syphilis.

White and Martin are of the opinion that reinfection with syphilis can occur, but that it is extremely rare, and that the majority of cases reported can be satisfactorily explained as recrudescences of the original infection. This opinion is in accord with my own. Fournier, than whom in his day there was no greater authority, states that reinfection is certain *only* when the following postulates can be fulfilled in their proper chronological order: A sore possessing all of the characteristics of a chancre, accompanied with inguinal adenopathy, which is followed some weeks later by a roseola or other syphilitic eruption and the characteristic symptoms of secondary syphilis—cephalalgia, alopecia and mucous patches; then a complete absence of tertiary accidents for a period of years. Should a chancre develop after this and be followed by incontestable secondary symptoms, as before, then a second infection may be inferred. The late R. W. Taylor states that as a general rule syphilis, like variola, scarlet fever and measles, attacks the individual but once in a life time, but that there are well-attested cases which seem to warrant the belief that in certain rare instances syphilis can and does attack a second time. Taylor also expresses the opinion that all putative cases should be approached with caution and reserve, and in order to establish the existence of a second infection the same general rules as laid down by Fournier should be observed. He considers no case worthy of consideration in which

the interval between the cure or apparent cessation of the first attack and the onset of the second is less than five years.

In this connection I quote the words of E. L. Keyes upon this subject. We cannot but admire the classic beauty of his phrases as well as the keen and deep insight which they show. "Syphilis once acquired stamps its impress upon the individuality of the patient and becomes a part of him, and no power on earth, in a given case, can say when the impress disappears. A half century may pass away and the trail of the serpent is still visible. This is a fact, and as such must be recognized. It is of vast importance, and to shut our eyes to it would be folly. That we do not shut our eyes, even those of us who believe in an early and radical cure of syphilis, is sufficiently shown by the avidity with which in doubtful cases of skin and bone disease the history of the patient is carefully inquired into for a record of preëxisting syphilis, which, if found, no matter how far distant, makes a diagnosis, establishes the treatment, and often leads to a cure. Yet, in spite of this assertion, who shall say that syphilis is not curable?

"Occasionally, cases are seen where syphilitic chancre is acquired a second time, followed by crops of secondary eruptions, and surely in these cases the old syphilis must have been cured, or the new case could not have occurred. The possibility of the duration of the effects of syphilis must be recognized by every intelligent physician who wishes to accept facts and desires to view syphilis in a practical light. The probability of the disease in most cases, however, is that its manifestations will disappear finally after a few years, and this under intelligent management becomes almost a certainty."

In discussing reinfection, Lydston of Chicago states that "Such cases are especially interesting both from their rarity and from the fact that they most conclusively prove the curability of syphilis." C. E. Marshall also states, "The curability of syphilis would appear to be proven by the occurrence of reinfection and it is probable that most attacks are cured."

The three eminent authorities just quoted are undoubtedly right. Reinfection does occur and the fact of its occurrence is absolute proof that syphilis is a curable disease. I am well aware that the contrary opinion is held by many physicians, but I do not know of a single syphilologist who holds this opinion. In my youth I remember it was said by the great Hayes Agnew that whoever had syphilis would have it all his life and his ghost would have it when he was dead. But our knowledge of syphilis has advanced greatly since Agnew's time and, besides, he was a surgeon and not a syphilologist.

Reinfection is undoubtedly the most satisfactory evidence of a cure that we have. But the mere healing of lesions does not

necessarily imply that the disease is cured or that the body has been sterilized to the treponemata. They may be driven to cover but somewhere, sometime, they will appear again unless it is proven by many Wassermann tests that the blood and spinal fluid are negative. Unless this be so the disease is not cured, even if symptoms are not present and have not been for many years.

We must be extremely circumspect in diagnosing reinfection, else we shall fall into error. In order, therefore, to establish beyond question a second infection the second case should be in agreement with the postulates formulated by Benario in 1914. These are:

1. Clinical demonstration of the primary sore.
2. Microscopic demonstration of the Treponema pallidum.
3. Glandular enlargement in the vicinity of the sore.
4. A positive Wassermann reaction.
5. The discovery of the source or medium of infection.

To this I would add that the patient must be known to have had a negative Wassermann reaction several times previous to the second infection. This last is absolutely necessary in order to prove that the patient was in a state of receptivity for another infection. If this is not proven it is impossible to state that a second infection has occurred. This is illustrated by a case reported by Western, in which a second chancre appeared while the patient's Wassermann was still negative. In November this patient presented himself with an indurated chancre. His Wassermann was positive. Neoarsphenamine was given, and in April of the following year his blood was negative to the Wassermann reaction. He was given, however, another injection of neoarsphenamine. A week later he had a coitus which was followed by a chancre in which the Treponema pallidum was demonstrated by dark-field illumination, and this second chancre was not on the site of the first. Now no one experienced in the treatment of syphilis would consider for an instant that this was a case of reinfection. If anything, it can be best explained by superinfection—a circumstance which rarely although at times undoubtedly occurs in the evolution of syphilis.

Superinfection in the second stage of syphilis is so rare as to be almost unheard of. I have searched the literature thoroughly and, except in the case just noted and one mentioned by Neugebauer, do not find it mentioned. However, in tertiary syphilis superinfection occasionally occurs. It is as if a new infection were grafted on the old and already existing one. A case reported by the Spaniard, De Agua, illustrates this very well. The patient had a papulo-gummatous syphilide on the forehead, for which he was treated by mercury salicylate intramuscularly and neoarsphenamine intravenously. The Wassermann was still positive after the lesion had healed and treatment had been discontinued. Nine

months later the patient acquired a primary sore although his Wassermann was still positive. In this case, while the old syphilis was still present a fresh infection occurred, as manifest by the second chancre. It will be noted in this connection that in such cases the postulates of Benario did not hold good. The evidence, therefore, is that superinfection can occur even after vigorous treatment and the new primary lesion may not appear on the site of the first, which if it did would come under the head of a chancre redux. It occurs also while the blood is still positive to the Wassermann reaction.

Let us now consider the postulate of Fournier that reinfection and superinfection do not occur until a period of years has elapsed. When syphilis was treated with mercury and potassium iodide such cases were most rare; and when they occurred it was not, as pointed out by Fournier and others of his time, until the disease had been in abeyance for many years. But since the advent of salvarsan, with its more potent action on the organism of syphilis, this no longer holds. A considerable number of cases of reinfection and also a number of cases of superinfection are now on record. I have seen quite a number, and others have had the same experience. It is no longer the rarity that it once was, although it must be admitted that these cases are by no means plentiful or common.

It is undoubtedly true that some individuals are less susceptible than others to infectious disease in general and to syphilis in particular; every physician of large experience is well aware of this truism. But that such a condition as absolute immunity to any infectious disease exists in any individual, I very much doubt. In regard to reinfection or superinfection in syphilis, it must be remembered, as Browning and McKenzie have remarked, that immunity in protozoal diseases, in which class syphilis belongs, is only short lived and if sterilization has been accomplished, as it undoubtedly has in not a few instances, reinfection can occur.

A case reported by Alderson goes far to show how completely the Treponema pallidum can be eradicated from the body, and following this a fresh infection occur. The patient was a woman with a typical chancre of the upper lip, which when he saw her first had existed for about a month. The presence of the treponema was demonstrated in the lesion. There was also a beginning roseola and other constitutional symptoms. The patient was also in the fifth month of pregnancy. She was given arsphenamine intravenously, and mercury and chalk 0.12 gm. t. i. d. was administered by mouth. A month later she was given another injection of arsphenamine. The chancre had healed and she showed no symptoms of the disease. Two months later she was given another injection of arsphenamine and three weeks later another. During the intervals between the injections she was taking by mouth mercury and chalk. Two weeks

after the last injection she was given potassium iodide for several weeks. At term she was delivered of a healthy child whose blood was negative to the Wassermann test. The mother was also negative for several weeks before the birth of the infant. Examination failed to reveal the presence of the treponema in the placenta or the cord. Five and a half months after her confinement the patient again presented herself with what was undoubtedly a second infection. She was suffering with a severe angina and generalized syphilides (their character was not stated in the report). She was treated with arsphenamine and her condition rapidly improved. The infant showed no signs of the disease and its blood was negative upon repeated examinations. This case, in my opinion, is one which offers the strongest evidence of any that syphilis is curable and also that when cured the disease can again be contracted.

While an individual who has had syphilis does not as a rule contract it again, this is not because a true immunity has been conferred by the first attack. In the vast majority of cases he does not contract the disease because, although clinically cured, he is not cured serologically, as evidenced by the positive Wassermann of his blood, although he has been, and may remain, free from all symptoms of the disease. But in spite of the known rebelliousness of the disease there are instances where reinfection occurs because it has been cured not only clinically but serologically as well, as shown by the negative Wassermann, which is the real criterion of a cure. It must follow, therefore, that the dictum of the great Ricord is not correct—"once infected with syphilis never again infected." Ricord based this upon clinical signs only, as he knew nothing of the Wassermann, and we now know that a clinical cure is misleading in so far as a real or serological cure is concerned. For the same reason the "laws" of Colles and Profeta are now obsolete. Unless cured serologically there can be no immunity to syphilis, but there is instead a relative insusceptibility of the skin and mucous membranes to a second invasion of the treponema as pointed out by Neisser, and even this may not always obtain; as witness the phenomenon of superinfection, that is, the occurrence of a chancre on an individual with a Wassermann that is still positive.

Since it is admitted that a second infection is possible and does occur, we must now consider the possibility of superinfection or the occurrence of a chancre while syphilis, active or latent, is still present in the patient's body, as determined by the Wassermann reaction. Undoubtedly many instances recorded as a second infection were really superinfection and for that reason, if no other, I am inclined to believe that superinfection is more frequent than reinfection. It was formerly believed that a chancre was not autoinoculable, but this belief in the light of modern knowledge has been

discarded. A large percentage of multiple chancres are the result of autoinoculation from an initial lesion which preceded them. Experiments conducted by Queyrat, by Taylor, De Maurignac and Neisser, prove beyond question that up to about two weeks after the appearance of the initial lesion other parts of the body surface can be inoculated from the original sore. When the secondary stage has become established there is then for a time at least an immunity to this superinfection that is extremely difficult to overcome. Ehrmann, however, succeeded in superinfecting syphilitics experimentally as late as six months after the appearance of the general eruption. At some of the points of inoculation he succeeded in demonstrating the presence of the Treponema pallidum. The lesions thus artificially induced partook of the character of the lesions then present on the patient's body. Finger and Landsteiner in their experiments also noted this peculiarity and, further, that lesions artificially induced in the tertiary stage resembled more or less true tertiary or gummatous lesions. It was also noted that these superinfections in no way influenced the course of the disease. From the experiments conducted by them, Finger and Landsteiner concluded that a syphilitic individual exposed anew, as it were, to infection may develop a local lesion, which is *not a true primary sore but a manifestation corresponding in character with a lesion which is typical of the stage of the disease as then existing in the patient.* This is in accord with the conclusions of Zinsser, Hopkins and McBurney that the resistance which develops in the course of the disease is an expression of localized tissue reaction as a result of an active invasion of the infecting organisms rather than as the result of an appreciable formation of circulating antibodies analogous to those observed in bacterial diseases. With these conclusions I am in full accord.

Before closing this chapter on what is perhaps one of the most interesting of the problems of syphilis, I desire to briefly discuss how far hereditary syphilis confers immunity against the acquired disease. We now know the reasons for Colles' and Profeta's laws—that the immunity in the mother and the child is not an immunity at all. The reason why they cannot acquire syphilis from each other is that they already have it. The question is—How long does the infection continue to exist in the patient with inherited syphilis? We know that it can extend even to the third generation. Does this inherited taint continue through life or does it gradually fade away and disappear? Tarnowsky has collected considerable data in regard to reinfection in hereditary syphilis. He has given it the name of "binary syphilis" and he believes that the disease superimposed, as it were, upon the inherited taint is much more baleful in its effect than when acquired by one who was previously

healthy. This might well be, when we consider the debilitated state of all of the tissues of the body which the inherited form of the infection would necessarily engender. Reinfection in hereditary lues has been reported by Boeck and by Taylor. It undoubtedly occurs, although I have never seen a case. According to Finger the pseudo-immunity conferred by hereditary syphilis passes away about puberty. That is the reason, perhaps, why cases of syphilis of the third generation are so very rare; and also because at puberty the sexual instinct is fully developed is why reinfection with the disease is then more apt to occur.

To sum up: Reinfection with syphilis can occur, and when it does it is absolute proof that the disease has been cured both clinically and serologically. When it occurs the second time the course of the disease is identical with the course of the first attack, although it may be somewhat milder. Because of the comparative rarity of the second attacks, phenomena pointing to such an attack should be very carefully examined and every possible test applied to establish the fact. Superinfection, or a primary lesion contracted by an individual already infected from another infected individual, also occurs. Such a lesion, however, is never a characteristic chancre but a sore which invariably partakes of the characteristics of the stage in which the recipient then is. Such being the case, a superinfection can always be distinguished from a true chancre. This superinfection has absolutely no effect, deleterious or otherwise, upon the progress of the current or original infection. Reinfection and possibly superinfection (although I am not acquainted with any mention of it in the literature), can also occur in individuals who have inherited syphilis. At puberty the majority of patients with inherited syphilis are free from the disease in so far as infecting others is concerned, although they may bear the result of their inherited dyscrasia through life.

CHAPTER XXI.

MALIGNANT SYPHILIS.

Syphilis as it is encountered at the present day is a comparatively benign disease in so far as its early clinical manifestations are concerned. I am of course not including its ultimate and far reaching results as exemplified by the lesions it produces in the brain and cord, the heart and other organs. In some instances, however, this benignity is reversed and we have a condition which is designated as malignant syphilis—a condition much less frequent now than formerly.

It has been supposed by some that malignant syphilis as we see it now represents a reversion to the early type such as was described by John of Vigo, von Hohenheim, Fracastor, and other writers of long ago. Others again have assumed that malignant syphilis is due to a special strain of treponemata more fulminant and virulent in their attack than those which produce the ordinary symptoms of the disease. Again, others have asserted that malignant syphilis is due to a peculiar lack of resistance of the tissues to the onslaught of the infecting organisms. Naegeli believes that malignant syphilis is due to an abnormal reaction of the tissues to the Treponema pallidum and that this reaction is allergic. In other words, he believes that there is an excess of antibody preëxistent in the tissues. This tendency to excess is probably inherent in the individual, as it can be explained in no other way. One or all of these opinions may be right because malignant syphilis has certain peculiar characteristics which make it an entirely different malady from the usual form of the disease.

Negative Wassermann.—One of the peculiar features and perhaps the most perplexing of all is the fact that many cases of malignant syphilis give a negative Wassermann reaction. I can recall a case in which the patient's palate was riddled with holes, the nasal bones necrosed, and yet in six different instances in which it was taken the Wassermann was invariably negative. Another peculiar feature is that the adenopathy so characteristic of ordinary syphilis is entirely absent in malignant syphilis. This has been observed by Fournier, Queyrat, Buschke and others. Ricord has stated that "adenitis follows the chancre as the shadow the body." But this does not obtain in malignant syphilis. In fact, even when the symptoms are most fulgurant there may be hardly any or no adenitis at all.

Lack of Secondary Symptoms.—Malignant syphilis is further characterized by the lack of secondary symptoms. The attack is so swift and terrific that these symptoms do not have time to develop as it were. Strange to say also, in malignant syphilis the mucous surfaces are comparatively immune. It is the cutaneous surfaces which largely bear the brunt of the attack. These in a general way are the chief points of difference between malignant syphilis and the ordinary type; but there is one other important point and that is, that contrary to what might be supposed, malignant syphilis does not respond to mercury. In fact many cases seem to be made worse by this specific drug. It responds better to the iodides, and best of all to arsphenamine; but even when this drug is exhibited it must be pushed to the utmost limit of tolerance before any beneficial effect can be observed.

Neisser has defined malignant syphilis as a severe form of the disease characterized by certain symptoms differing rather in their nature than in severity from the usual form of the disease. For that reason every case of severe syphilis should not be included under the designation of "malignant." For example, an attack of syphilis may be rendered extremely dangerous because of the organs attacked or by reason of some preëxisting morbid condition, as when the disease attacks the nervous system or when it is complicated with tuberculosis. To cases of this kind the term "syphilis gravis" is more appropriate. Malignant syphilis should also be separated from early tertiary manifestations known as "syphilis tertiaria præcox," although it must be admitted that malignant syphilis is characterized by the absence of the secondary stage of the disease.

Malignant syphilis is applied to those cases which are fulminant in type, in which the ulcerative processes appear precociously and are destructive from the onset and which resist treatment to a greater or less degree. It has also been noted in this type of lues that when the disease has spent itself as it were, it does not show the proneness to recur which is so often manifest in syphilis of the ordinary type. Thus malignant syphilis may be represented as a pathologic storm succeeded by a calm.

Fournier and Bassereau have asserted that when the chancre early assumes a phagedenic character that syphilis of the malignant type is most apt to follow. This does not always obtain however, as cases have been recorded in which the initial lesion was seemingly benign as compared with the subsequent constitutional symptoms. Nor does the state of the patient's health always explain the development of the malignant type of the disease, for many victims of malignant syphilis when they acquire the disease are in robust health. It has been suggested as an explanation of the occurrence

of malignant syphilis in some subjects that their ancestors have been comparatively free from the disease and therefore the seed falls upon a virgin soil as it were; but after all, this affords only a partial explanation for the number of benign cases of syphilis occurring on so-called virgin soil far exceeds the number of cases of malignant syphilis.

As to there being a special strain of treponema which is particularly virulent, as suggested by Hutchinson, it has been shown by Lesser that malignant syphilis may be contracted from a patient whose syphilis is benign and that benign syphilis may also be contracted from malignant syphilis.[1]

Neisser maintains that the exceptional constitutional and local symptoms of malignant syphilis both prove that we are confronted with what is an unusual relation or rather reaction, between the treponemata and the tissues of the affected individual; in other words, that it is a question of tissue resistance to the treponemata. He therefore concludes that malignancy manifested in syphilis is due entirely to the peculiar susceptibility of the individual acquiring the disease. The susceptibility shows itself by the rapid destruction of the syphilitic granuloma, which otherwise disappears only by a slow process of evolution and by the excessive reaction of the bodily organism against the toxins generated by the infecting agent. This sensitiveness of the individual is a special phenomenon and must not be confused with debilitating conditions which would otherwise modify the course of the disease and induce the condition already mentioned as "syphilis gravis;" such debilitating conditions are alcoholism, gout, scurvy, diabetes, nephritis, tuberculosis and any other enervating cachexia. With Neisser's opinion I agree.

Constitutional Symptoms.—All cases of malignant syphilis are characterized by constitutional symptoms of a severity far in excess of those which usually occur in the course of the disease. These symptoms are fever, which may closely simulate the typhoid state; anemia, which is marked, the blood picture resembling that seen in chlorosis rather than the anemia of the so-called pernicious type. Insomnia is also a prominent symptom; this is probably due to the cephalalgia which is nearly always present to a prominent degree. These patients are also markedly cachectic; they are emaciated, and show all of the evidences of a profound toxemia.

In malignant syphilis the mucous surfaces are comparatively exempt but this by no means applies to the cutaneous surface of body; for it is upon the cutaneous surface that the fury of the disease is seemingly expended. Here are presented extensive and irregularly distributed lesions of various types. These consist of

[1] See "Strain in Spirochetes," by Burton Peter Thom, M.D., in The American Journal of Syphilis, vol. v., January 1921.

large papules and nodes which very quickly break down and form ulcers, many of which are extremely destructive. Many of these ulcers become infected with pus forming organisms and thus give rise to rupial and other crustaceous skin lesions. These ulcerating lesions show a remarkable predilection for the face and scalp. Bone lesions are also not uncommon and are very destructive and disfiguring especially if the nasal bones are attacked. Ulcers occurring in the neighborhood of large vessels may cause severe hemorrhages which of course add to the patient's anemia.

As I have already stated, it was formerly supposed that phagedena of the chancre presaged malignant syphilis. While it undoubtedly does so in many instances it does not always follow. The lesions of malignant syphilis in many instances show phagedenism but, as has been pointed out by Tarnowsky, these cases are often due to a mixed infection with pyogenic cocci. This may be true in some instances but I agree with Neisser that it does not completely explain the lesions of malignant syphilis.

Syphilides.—Some cases of malignant syphilis from the onset show a pustular rash which is attended with ulceration and with scab formation. The ulcers are deep, with undermined edges and a base from which is secreted a fetid pus. This type of eruption as a rule first invades the face and scalp and later may attack the arms, legs, and trunk. The tendency so often seen in syphilitic eruptions to form in circinate groups is not seen in malignant syphilis. In some instances there is the formation of tubercles which quickly break down into ulcers which become covered with a thick crust. In this form of eruption the destruction of tissue and consequent scar formation is much greater than in the pustular variety. The invasion of the eruption is usually rapid but occasionally may be slow, taking a number of months before it reaches its maturity.

Another type, and by far the most formidable of all because it invariably produces such a profound cachexia as to endanger the life of the patient, begins with large tubercles of a deep, coppery red color. A black slough forms in the center of the tubercle. At first it is firmly adherent but soon becomes loosened and increases in size and is cast off as a fetid mass, leaving a deep crater-like ulcer from which exudes a thin and foul-smelling ichorous pus. These ulcers are surrounded by a deep colored areola; and they frequently become phagedenic, which further complicates matters.

Gummata.—In some instances malignant syphilis appears as precocious gummata. These appear at the time that the secondary eruption should occur, but in malignant syphilis there is practically no secondary stage. These gummata appear as small circumscribed swellings, painless and imbedded in the skin. They soon become red and then look not unlike blind boils. They grow rapidly and

darken in color to a coppery hue. At first they are quite hard but later they become soft. They may or may not go on to ulceration. Should ulceration occur they soften more rapidly and become necrotic in the center and this necrosed area sloughs off leaving an ugly ulcer with a greenish floor, from which exudes sanious pus. These precocious gummata as seen in malignant syphilis, are as a rule, not as deeply seated as those which may be termed true tertiary gummata. There is also a neurotic form of precocious gummata noted in malignant syphilis and preceded by severe neuralgic pains or accompanied by the same. The nerves involved are the cranial and facial nerves, the intercostal and the anterior crural. These pains may be continuous or intermittent and are sometimes of excruciating severity. The gummata accompanying this nervous type are sometimes quite large. They may ulcerate but as a rule, after a longer or shorter period, they resolve. Along with the pain there is also fever, emaciation and the concomitant symptoms of a severe toxemia.

It has been assumed that malignant syphilis occurs only in the cachectic, such as those who acquire the disease while they are already suffering from some other disease, such as tuberculosis or diabetes or some chronic metabolic dyscrasia. That this lowered state of bodily resistance predisposes to a malignant form of syphilis cannot be denied. But as I have already stated it not infrequently happens that individuals who contract syphilis, while seemingly in the best of health, sometimes manifest the disease in its severest and most precocious forms. A peculiar fact to which I call the reader's attention is that those persons who are auburn-haired seem to stand syphilis badly. I have never known a man or woman with red hair who when they acquired syphilis did not take it in a severe form. Yet I also have noted that those acquiring syphilis when they are past middle age also seem to have a more severe form of the disease than those who acquire it earlier in life, although this does not always hold good.

Malignant syphilis is always ulcerative and destructive, and for that reason its lesions may be compared with precocious tertiary lesions, and I personally regard malignant syphilis as nothing more than a precocious appearance of the third stage of the disease. However, there are those who have asked the question "Is malignant precocious syphilis really syphilis?" This question was first put by Queyrat in 1908, and Carle in 1911 propounded the same question. My opinion is that it is syphilis which has fallen upon a peculiarly fertile soil, that is, has been acquired by an individual whose tissue resistance is peculiarly susceptible to the ravages of the infecting organism. That it is, or may be, a separate and distinct disease entity, I absolutely deny. Malignant syphilis usually

runs an extremely rapid course. The symptoms are intense and the resulting mutilations are ofttimes most severe. The disease invariably goes from bad to worse and does not respond to treatment or hygiene. In fact, some of these cases pass into such a condition of cachexia and prostration, that death results, although I wish to go on record as saying that death from syphilis *per se* is a most rare occurrence. However, although the patient is for the time saturated, as it were, with the disease, a recovery not infrequently occurs, and strange to say, these patients seem to be ever after remarkably free from any tertiary manifestations of the disease.

Another peculiarity of malignant syphilis is the fact that there is a total want of sequence or of chronology in the symptoms. The chancre may be phagedenic, and before and while it is still present, colossal lymphangitis and gangrenous ulcers may be present elsewhere. No secondary lesions, as we know them, being present, only fulminant tertiary lesions are seen. These cases do not respond to specific treatment, and to those who have seen the marvelous results of intensive specific medication, the unfavorable reaction of these cases to that medication which our experience has taught us to be absolutely curative of syphilis, presents a paradox; and the moral effect on the physician is very marked, for we are frequently at our wits' ends to know what to do. Let us take into consideration the action of mercury on malignant precocious syphilis. This drug is worse than useless in this type of the disease, and in those malignant precocious cases in which the patient does not respond to mercurial treatment, its use should be stopped at once, because it does more harm than good. I have yet to see a beneficial result occurring in malignant syphilis where mercury was administered, no matter how it was given. This is not only my own experience, but that of Queyrat and also of Griffon and Ducastel. These cases respond better to the arsenicals than to mercury, but even this powerful agent in some cases seems to fail.

Iodide of potassium, from the very nature of the lesions, perhaps, seems to give better results. I agree with Queyrat that the only way to treat these cases is to let them alone so far as specific medication is concerned, and to treat them only by such hygienic methods as are available. Another very peculiar feature about the malignant syphilis is that along with a negative Wassermann there is also the absence of treponemata in the material taken from the lesions.

There is a type that may be described as malignant syphilis in which, while the symptoms are not so severe, they yet fail to respond to specific medication as the disease otherwise almost invariably does. These cases also are a mystery which I shall not attempt to explain. It is to be noted that all cases of phagedenic chancre are almost invariably followed by malignant symptoms. As a rule,

malignant precocious syphilis does not run a prolonged course. The attack is short and sharp. Surface lesions run their course in about six months; internal lesions last about twice as long. The mucosæ are seldom attacked, but when they are the lesions are apt to be extremely severe. There is also, as it would be natural to infer, severe constitutional reaction. This may even simulate a typhoid state and the patient may die therefrom. It is of interest to note that those cases of malignant syphilis in which the adenopathy is marked, offer a better prognosis than those in which there is no such enlargement. Many of these cases develop the symptoms of iodism. This is because the drug has been exhibited in large doses in the hope that it will influence the lesions where mercury or arsphenamine have failed. Following the use of iodides in malignant syphilis, fatal edema of the glottis has been known to occur.

Malignant syphilis is, of course, a generic term, and the different forms in which the disease appears early or late are usually grouped together in bibliographies. The term "galloping" syphilis has a somewhat different connotation but is usually synonymous with malignant precocious syphilis. In my opinion there is no difference and the terms mean the same thing. Some consider "syphilis gravis" as an apparently less severe form than the malignant precocious type. "Virulent syphilis" is the word usually employed to describe malignant precocious syphilis in Great Britain. Not infrequently, malignant precocious syphilis manifests itself by lesions of the nervous system. These cases usually manifest themselves by the appearance of an early syphilitic meningitis which is frequently fatal.

Again under this caption of malignant precocious syphilis, we note cases which occur from time to time of the flaring up, as it were, of an old focus of the disease, either in a congenital syphilitic or in one who has had the disease for a long time. In these cases the action of the infection behaves very much as it does in the primary form. This manifestation of the disease proves as rebellious to treatment, and as destructive, as the malignant precocious form. In other words, I may say that these cases represent what may be termed "late" malignant syphilis. Death is not infrequently the result in these cases. This affection of course is not precocious in so far as chronology is concerned, but the malignancy is just as apparent as in the accepted form of this type of the disease. In these advanced cases in which there is a malignant recurrence, there is almost always a pronounced toxemia, which may be the cause of death.

Neisser seems to consider malignant precocious syphilis as an anomalous secondary stage in which instead of macules and papules, pustules and ulcers occur. These ulcers he does not consider gummatous and thus he differentiates from precocious tertiary syphilis.

Joseph and Lesser differ from him and see in malignant precocious syphilis an early gummatous syphilis which will attack the bones as well as the skin and mucous surfaces, for Neisser has claimed that in malignant precocious syphilis only the skin and mucous surfaces suffer. Finger has attempted to reconcile these two views, but not with success. I am inclined to view the matter in the same light as Joseph and Lesser.

As already stated, malignant precocious syphilis as a rule expends its force in a comparatively short time, when we consider the usual chronicity of the disease. However, cases have been reported in which the malignancy, characterized by ulcers and destructive lesions which were rebellious to treatment, had persisted as long as ten years. Epstein mentions a case which comes under this category and which may be termed precocious "inveterate" tertiary syphilis, if I may be allowed to coin that term.

Occasionally malignant precocious syphilis is characterized by lesions of the internal organs, such as the liver and the brain. In these cases an intense jaundice may appear, accompanied by meningeal symptoms. Death in coma usually follows. A form of syphilis which we might consider here is that which has been described by Kurnitzky. This is malignant reinfection; or in other words, we will assume that the patient has been cured of syphilis and again acquired the disease, which by our present methods is quite possible. His second attack is characterized by ulcerous cutaneous lesions of great severity, which are rebellious to the usual treatment; and the disease runs the same course and shows the same characteristics as it did when it was primarily incurred. Neisser also reported a case of superinfection occurring in malignant lues. It is apparent, therefore, that in very rare instances the infective organism sensitizes the patient, as it were, and produces a malignant type, which *per se*, is not natural to him.

Malignant syphilis is not seen as frequent as formerly. Death from malignant syphilis, which undoubtedly occurred in the ancient syphilologist, Ulrich von Hutten, is today a most rare occurrence. The reasons for this gradual disappearance of the malignant type of the disease are, undoubtedly, the gradual attenuation of the virulence of the treponemata, and the increased resistance of the individual because of the long incidence of the disease amongst civilized man; for, as Neisser has truly said, civilization and syphilization go hand in hand. Another reason for its gradual disappearance is the present improved method of treatment; and this last is in my opinion the most important factor in the subsidence of malignant syphilis.

CHAPTER XXII.

CONGENITAL SYPHILIS IN THE ADULT.

Every physician in active practice is more or less acquainted with hereditary syphilis as it occurs in infancy and childhood. He also with more or less frequency comes in contact with those hereditary manifestations of the disease known as *syphilis hereditaria tarda*. The hereditary syphilis occurring in the adult, which I propose to discuss here, is not, however, as the reader at first glance may suppose, this form of delayed syphilis. As understood by modern syphilologists *syphilis hereditaria tarda* implies such manifestations as relapses and is a synonym of late relapsing syphilis. I shall consider, therefore, the form of hereditary syphilis which *first* appears at maturity. The lowest limit being twenty years in males and eighteen years in females. These cases are sufficiently numerous to merit careful consideration, although they are much less frequently encountered than those preceded by manifestations in childhood. It is because of this and because they are often unrecognized and given different labels, that I shall here discuss this little known phase of hereditary syphilis.

Many of these patients are healthy and free from the stigmata of hereditary syphilis until the time of outbreak. No limit can be set to the time of outbreak.

Occurrence.—Cases have been known to occur after sixty years of age. As in acquired syphilis no organ or tissue of the body is exempt. As in acquired syphilis the nervous system is most frequently involved. This should occasion no surprise, as it is well known that the Treponema pallidum is the most potent causative factor of all organic disorders of the nervous system. Next in the order of occurrence are the integumentary structures, the bones, the eye, throat, cellular tissue, joints, liver, and genitals.

Symptoms.—As in the acquired form of the disease, the manifestations of involvement of the nervous system in late hereditary syphilis are varied. Headache may be the sole symptom. It is a common symptom in inherited syphilis but in these cases it comes on at a much earlier age. It may be associated with insomnia. These patients almost invariably have stigmata of congenital syphilis. In passing, I might add, that in such cases relief comes very quickly when potassium iodide is exhibited.

Epilepsy.—Epilepsy in some instances is undoubtedly a late congenital symptom. It may be general or focal. It must not be confounded with the convulsions in the early stage of paresis developing in late hereditary syphilis. Hemiplegias due to different mechanisms such as embolism, apoplexy and softening are not uncommon. Paralyses due to lesions of the peripheral nerves are also of frequent occurrence.

Tabes Dorsalis.—For many years it has been known that tabes develops in some instances in heredosyphilis. There is no difference in so far as symptoms are concerned between that due to acquired syphilis and that which occurs as a late hereditary manifestation. In acquired syphilis tabes usually appears in patients of mature years, whereas the incidence in the inherited form is somewhat earlier. Since the period of latency in tabes is unknown and as many tabetics seem to have no idea of the syphilitic causation of their malady, it is therefore quite possible that some of them are suffering from the hereditary form of the disease.

Tabes in congenital syphilis sometimes occurs at a very tender age. A case is even on record of an infant having been born with the disease.

The statement just made that the tabes of acquired syphilis does not differ from the hereditary form needs some qualification, in so far as in the hereditary form there are marked premonitory symptoms which are not present in the acquired form. In late congenital tabes there is invariably a history of neuroses not only affecting the patient previously but also in his ascendants and collaterals. These neuroses are so common as to be absolutely significant. This is to be noted in tabetic brothers and cousins. In short, these heredotabetics are preëminently of neuropathic stock and are themselves, long before the development of the tabetic symptom complex, of neuropathic tendencies.

Paresis.—Although a fact that it is little known, paresis is in rare instances a terminal in late hereditary syphilis.

Neuropathies.—The neuropathies which usually afflict this class of patients most frequently take the form of hysteroid states and neurasthenia. Complicating these in many instances are phobias and obsessions which may later become dementia præcox. A strange fact is that a family, in which this syphilitic neuropathic taint is very strong, will almost always have one member who is entirely free from stigmata of any kind.

Cutaneous Lesions.—The next most frequent form in which late hereditary lues shows itself is in cutaneous lesions. For some unknown reason they are much more common in women than in men. With very few exceptions they appear as ulcerated gummata. Occasionally they take the form of a tubercular syphilide. These

may be regarded as an attenuated form. These lesions display no differences from the tertiary lesions of the acquired disease. The entire integument may be infiltrated and on this base ulcers may form; or the lesion may appear as an isolated and circumscribed ulcerating gumma. These lesions may endure for many years and even when finally healed not infrequently return. The surface involved may be very large—perhaps an entire leg. When we consider that these patients may be free from all inherited stigmata it is sometimes difficult to believe that we are not confronted with acquired syphilis in the tertiary stage.

As a rule the diagnosis of these lesions is not difficult. When appearing on the face they may at times be confused with lupus, but the punched out appearance of the ulcer and the black crusts covering it will usually be sufficient to confirm its syphilitic nature. In others the circinate configuration will tell the story. In some instances, however, the diagnosis is not so easy. Lupus and scrofuloderma may be so closely simulated that we may be justified in calling them scrofulo-syphilides. While some are inclined to doubt the existence of these hybrids, as it were, I am convinced that a true disease association does exist.

Occasionally in late hereditary syphilis lesions partaking of the nature of secondaries may appear. They are usually present as papules. They may or may not be associated with lesions of the tertiary type. Superficial gummata when occurring on the leg or arm, as they not infrequently do, may become complicated with lymphangitis or phagedena. When lymphangitis occurs pseudo-elephantiasis sometimes follows in which a hard edema occupies the entire leg or arm. The phagadenic type is sometimes extremely difficult to diagnose from tuberculosis.

Ulcers.—When these ulcerating gummata are situated on the leg they simulate the ulcers caused by varicose veins very closely. They begin as gummatous ulcers but as time goes on and the veins and lymph channels become involved, a true varicose condition of the leg supervenes. This transformation is but a natural sequence for varicose ulcers originate from any cause which produces a venous stasis.

Genital Lesions.—Genital lesions occurring in late hereditary syphilis technically come under the heading of lesions of the tegumentary structures. Ulcerating gummata occupying these parts both in the male and female are almost invariably accompanied with phagedena and are often horribly destructive. In men these lesions are sometimes confused with chancroid, and in women with ésthiomène (which see). They are much less frequently met with in women than in men. Whenever one of these lesions is encountered on the male or female genitals, unaccompanied by

any other of the phenomena of syphilis—especially if phagedena is also present—late hereditary syphilis must always be considered.

Bone Lesions.—Lesions of the bones are not uncommon in late hereditary syphilis. Not a few cases of so-called tuberculous bone disease are undoubtedly caused by the Treponema pallidum rather than by the *tubercle bacillus.* Late hereditary syphilis of the bone may express itself as Paget's disease or osteitis deformans. It may express itself as a universal bone-ache with no definite location. In this instance the pain is worse on motion. Dactylitis, so often met with in inherited syphilis of infants, may also occur as a symptom of delayed hereditary syphilis. Necrosis and consequent sequestrum formation may occur; and this may be mistaken for a tuberculous process. As a rule these syphilitic conditions yield rapidly to treatment in which they differ markedly from those caused by the tubercle bacillus.

Ocular Lesions.—Ocular lesions in late hereditary syphilis are not infrequent. This does not include disorders of central nervous origin or of the bones of the orbit. The condition most frequently encountered is keratitis. The iris, choroid and retina may also be involved. It is to be noted that there is evidence of a tendency for ocular and joint affections to coexist. In addition to the parenchymatous keratitis, which is the condition most frequently observed, there is also a neuro-paralytic form which is rarely seen.

Ear Lesions.—In late hereditary syphilis, the ear for some reason seems to be comparatively free from attack; but this does not mean that such attacks never occur. In childhood and youth suppurative disturbances are those which are most apt to occur; in adult life—the true period of late hereditary syphilis—lesions involving the labyrinth are the rule, deafness and tinnitus, vertigo and vomiting—the picture known as Ménière's disease. These conditions may come on rapidly and without any premonitory symptoms. The course may be acute or very protracted. There is no direct way in which the diagnosis can be made except by the Wassermann, as these symptoms may be caused by conditions other than syphilis. Treatment in these cases must be inaugurated promptly, as little can be accomplished after destructive changes have taken place.

Lesions of Mouth and Nose.—Lesions of the mouth and nose, differing in no wise from the tertiary lesions which not infrequently attack these parts in acquired syphilis, are not uncommon in late hereditary syphilis. They usually appear as gummatous ulcers which may cause much destruction and disfigurement. They include the velum palati, denudation of bones and necrosis with elimination of sequestra, gummatous osteomata, chronic suppuration, perforation of the nasal septum, destruction of the nasal bone with sinking of the bridge—"saddle nose"—and destruction of the

turbinates. These affections begin insidiously and their evolution consists of two stages; the first ill defined and mild, the second severe and destructive. The latter are very apt to come on so suddenly that irreparable damage is done before treatment has a chance to stay the process of destruction. It often happens that during the mild stage when treatment would be efficacious, syphilis is not suspected. The tongue is rarely attacked in late hereditary syphilis. This is passing strange, since it is quite common for this organ to be the seat of gummatous deposits or leukoplakia in tertiary syphilis that has been acquired. When leukoplakia, however, occurs in an individual who has not reached middle age, late hereditary syphilis is to be suspected very strongly.

FIG. 63.—Congenital syphilis (condylomata). (Courtesy of Dr. M. B. Parounagian.)

Joint Lesions.—Affections of the joints are comparatively common in late hereditary syphilis. They are more frequent in women than in men. The lesions occurring in late hereditary syphilis are identical with those occurring in younger subjects and which, in them, are grouped as pathognomonic of heredosyphilis. Osteoarthritis, a form of syphilitic "white swelling," osteophytes, or bony outgrowths, and a form of pseudo-arthritis deformans, are to be included in the joint lesions of late hereditary syphilis. It is needless to state that the diagnosis of these conditions is of extreme importance because of the prognosis, which in lues is invariably hopeful. Included in the osteoarthritis just mentioned is bilateral synovitis, which in this instance is rather more than a simple synovial effusion; in my opinion it represents a low grade of epiphysitis. In passing, I may add that bilateral synovitis of the knee is also seen in acquired syphilis.

This osteoarthritis is in reality a fibrosynovitis, the cell infiltration being distinctly gummatous. The joint is not involved en masse

but rather in foci—small tumor like masses of cartilaginous hardness being imbedded in the reflexions of the synovial sac. The swelling of the joint is caused by a secondary hydrarthrosis. While imitating "white swelling" very closely the fungosities occurring in this condition are entirely absent. As in the tuberculous process the onset is insidious. Disability is rarely complete and if the knees are the joints affected the patient can usually get about, although with difficulty. Vicious attitudes or contractures do not occur. However, in time contractures may take place. Occasionally these joint lesions are complicated with fistulæ or abscesses, when they may be mistaken for tuberculous inflammation. Gaucher and Mannino both relate cases which were remarkable for their close simulation of a tuberculous process, but which rapidly healed under the influence of antiluetic treatment.

Exostoses.—Another form of joint syphilis, to be found in the late hereditary type of the disease, is that caused by the formation of exostoses on the epiphyses of the long bones—usually those composing the knee joint. The clinical appearance resembles" white swelling." The illusion ends here, however, for on palpation there is no bogginess but instead bony excrescences are felt everywhere in the joint.

Pseudo-arthritis Deformans.—The so-called pseudo-arthritis deformans is but rarely encountered. It is due apparently to the formation of osteophytes close to the articular surfaces so that movement is much hampered. This process is progressive and symmetrical. It attacks usually the hands and feet, so that its resemblance to the other or lithemic form of this symptom complex is very close indeed. At times it produces extreme deformity of the hands and feet.

Lymphatic Involvement.—Involvement of the lymphatic nodes is common in late hereditary syphilis. In most instances it is gummatous. These gummata do not always break down and ulcerate, however, but remain cold and indolent for years. It is extremely difficult to distinguish them from strumous glands. Their location corresponds exactly to that of strumous glands, hence the mediastinal and mesenteric glands may be involved. I am convinced that many cases of struma as so exemplified are late hereditary syphilis.

Visceral Involvement.—Late hereditary syphilis, as in the tertiary phase of the acquired disease, attacks the viscera—the heart, lungs, liver, spleen and kidneys. It is my opinion, based upon personal observation, that many cases of cardiac disease occurring in subjects under thirty-five years of age, with no previous history of rheumatism, are due to late hereditary syphilis. The contention is difficult to prove, perhaps, but nervetheless I am convinced of its being the fact. Syphilis of the lungs simulating pulmonary tuberculosis has been reported by Lancereaux and Fournier. Its occurrence is very rare. I cannot recall having seen a case occurring in late hereditary

syphilis. Late hereditary syphilis is undoubtedly the cause of some cases of hepatitis of the hypertrophic type. Gummata occurring in the liver substance have also been known, as well as amyloid degeneration.

Similar pathologic changes have been noted in the spleen and kidneys.

Late congenital syphilis in many respects presents some of the most abstruse problems that confront the physician. If it was suspected more often than it is many an ailing man and woman would be restored to health. As a dyscrasia it is if anything more occult than when the disease is acquired. Its existence in a latent form from the beginning of life enables it to exercise a profound if secret influence upon every organ and tissue of the body, and this influence is invariably depressing. As has been pointed out by Rolleston, this reduced resistance makes these patients an easy prey to secondary infections of a chronic character and so renders the treatment of the resulting disease more complex, and less satisfactory. Glandular tuberculosis and hypothyroidism can in many instances be explained on this basis. It is more than probable in my opinion that many endocrine affections when not due to acquired syphilis can be traced to this form of syphilis. When we consider the pathology of syphilis it would be remarkable, as Rolleston says, "if the ductless glands escaped syphilization." One gland alone is rarely affected and the diagnosis is more difficult in the presence of a polyglandular dysfunction. The adrenals, the pituitary and testes are the endocrine glands most frequently affected by late congenital syphilis. A most frequent syndrome being that which the French designate as "Addisonism" which is a form of adrenal insufficiency which is most frequently encountered and most infrequently diagnosed. What physician does not have those patients who are always ailing, whose muscular tone has always been below par, who have just sufficient vigor to keep them out of bed, and whose arterial tension is always low?

In diabetes insipidus, Frolich's adiposo-genital dystrophy and thyroid dysfunction, think of late congenital syphilis—the congenital syphilis that is masked in childhood but which openly or —more often—covertly attacks the adult. As has been conclusively shown by Castex and Del Valle chronic abdominal symptoms, such as are caused by pericolitis and perienteritis or the condition described by Lane, Jackson and Wilms are not infrequently manifestations of late congenital syphilis.

Thus it will be seen that late congenital syphilis is a mask for many conditions—especially those in which the cause is obscure or which are atypical in their course. For this reason syphilis, because of its superlative tendency to protean attack, should always be suspected.

CHAPTER XXIII.

SYPHILIS OF THE THIRD GENERATION.

In the domain of heredosyphilis there is no problem in which there is so much uncertainty, and concerning which so much skepticism has been expressed, as the possibility of the transmission of syphilis through three successive generations. Connubial infection passes away, except in very rare instances, in about ten years, and it would, therefore, seem rather improbable that a child born syphilitic should retain the power of transmitting the disease to its offspring when it had reached maturity. Yet the transmission of syphilis to the third generation is an accepted fact to a formidable array of authorities.

The great Paracelsus was the first to assert that syphilis could be transmitted by inheritance. But it was not until nearly two centuries later that the fact of the transmission of the disease from parent to offspring was generally accepted. The names of Van Helmont in the sixteenth and Rankin and Sanchez in the seventeenth century stand out as believers in the transmissibility of syphilis through several generations.

Since then many cases have been reported, but all of them contain lacunæ of detail which hinder the establishment of the fact. It is easy to understand why convincing cases are few and far between, when we consider that the infirmities of their inherited disease prevents many of these victims of their father's sins from marrying and so transmitting their dyscrasia to their children in the third generation. Also, it must be borne in mind that the cases are necessarily spread over long spans of years, that death, misrepresentation, and the vicissitudes of life, make the acquirement of the facts of this phase of lues difficult in the extreme. Yet there are cases on record which are most illuminating and convincing, and it is more than strange that their import and significance has not long ago been recognized.

Jonathan Hutchinson—who afterward denied the transmission of syphilis to the third generation—in 1865 reported two cases of heredosyphilitic children, the issue of undoubtedly heredosyphilitic mothers. The first was a female child of five years with chronic syphilitic synovitis of the left knee. The mother, because of her characteristic syphilitic physiognomy, attracted Hutchinson's attention immediately. Her corneæ were clouded by a past kera-

titis. The bridge of her nose was sunken and her complexion was pale and earthy. Her teeth were typically malformed. In other words, she presented to this keen observer the appearance of a typical congenital syphilitic, which undoubtedly she was. She stated that she had but this one child and that she never had any others, nor had she any miscarriages.

The second was an infant born to a woman who came under Hutchinson's treatment for syphilitic keratitis. She was twenty-one years of age, and had been married a year, and was then nursing her first child. In addition to the keratitis, she presented other unmistakable evidences of inherited lues. She had notched teeth, and there were radiating scars at the angles of the mouth, and her forehead was knobby and protuberant from past periostitis. The infant of this woman had obstructed nostrils and its buttocks were covered with copper colored scaly patches of the most unmistakable character. Further, to complete if possible the chain of evidence, these symptoms all disappeared under treatment with mercury and the child to all intents and purposes became well.

Before Hutchinson's time our knowledge of congenital syphilis was vague, to say the least. Beyond the fact that it existed, and that in its early stage it showed itself as an exanthem on the buttocks and elsewhere, little else was known of this important phase of lues. It is due to this eminent English syphilologist that hereditary lues began to be studied with the scientific acumen which hitherto had not been accorded it.

About the same time that Hutchinson reported his cases, W. Boeck also reported a case equally as interesting as the two of Hutchinson. In 1854, the grandmother, representing the first generation, at the age of eighteen was treated for "ulcers of the genital organs, universal roseola, and opalescent patches on the right tonsil;" in other words, for secondary syphilis. She left the hospital in two months. In 1860 she brought to the hospital her daughter two months old, who was treated by Boeck for congenital syphilis of a severe character for a period of four months. Three years later this child was again treated by Boeck for a syphilitic affection of the eyes. Twenty-six years later—in 1889—this same child again came under Boeck's observations. She bore indelible traces of the congenital syphilis with which she had been afflicted in infancy. There were the radiating scars at the angles of the mouth, notched and pegged teeth, and traces of a former interstitial keratitis in both eyes. There was also an almost complete occlusion of the iris of the left eye. At the same time she brought her son, an infant of five months, representing the third generation. The infant had syphilitic coryza and well marked palmar and plantar syphilides. The father was examined but showed no signs of the

disease. The child in question was the second, the first showing no evidences of the disease. Also there was another healthy child begotten by another father a year before her marriage to her husband. Boeck did not believe that the question of paternal heredity entered, as it is known that occasionally healthy children precede syphilitic ones.

Edmond Fournier has described the following case in support of the transmission of active syphilis to the third generation. A young man aged twenty-two years, had an extensive tubercular syphilide of the thigh, which had been present since the age of five years. He also had multiple stigmata of heredosyphilis, including both dental and ophthalmic stigmata. The father of this patient also exhibited signs of hereditary syphilis, including evidences of a past keratitis and other ophthalmic lesions; the teeth also indicated hereditary lues. His mother, the grandmother of the first patient, after having two healthy children, suckled a strange infant which died "with large suppurating sores on the body." Soon after this a sore developed on her breast, followed by sores on her body. The infant she was then suckling also developed similar sores and died in a few weeks. She afterward suffered from severe headaches and eventually died of hemiplegia. Two years after this infection the child was born who was the father of the original case. From this Fournier concludes that the grandmother contracted syphilis by suckling a syphilitic infant; and further, that the evidence showed that acquired syphilis was absent in the father and son, and that the case fulfills all the conditions necessary to demonstrate the transmission of both the dystrophic and virulent effects of congenital syphilis to the third generation.

The younger Fournier also quotes the following: The grandfather contracted syphilis and his son had congenital syphilis. He married a healthy woman. The marriage resulted in 15 pregnancies, of which 5 ended in abortion, 2 infants died shortly after birth, and 8 survived. Of these, 1 appeared healthy, 6 had stigmata of congenital syphilis, and 1 had besides these dystrophic evidences of the disease ulcerations on the buttocks and in the mouth, and perforation of the soft palate.

Two Varieties of Heredosyphilis.—Edmond Fournier has collected 19 similar cases, in which, he believes, all the conditions required to prove the transmission of syphilis to the third generation, have been fulfilled. In some of the cases herein detailed the evidence does not seem to be absolutely complete, yet it is sufficiently strong to make it, to say the least, extremely probable. Moreover, it is to be noted that from the cases cited it would seem probable that there are two distinct forms of syphilitic transmission to the third generation, one of which is not uncommon and if watched for

will be observed by all men of wide experience, the other is most rare. These two forms of syphilitic disease transmitted to the third generation are the dystrophic and the active. That is, one form shows stigmata and no lesions, while the second and by far the rarer form may show both, that is, dystrophies and active lesions as well.

The Dystrophic Form of Heredosyphilis.—Edmond Fournier has prepared the following synopsis of dystrophies which mark the syphilitic child in the third generation. I desire to say that I am not wholly in accord with the doleful picture which he paints. While these undoubtedly occur, in my opinion they are more apt to be encountered in the second generation than in the third when the disease has all but spent itself as must necessarily be the case. He enumerates meningitis and the convulsive habitus, dental stigmata, ophthalmic stigmata, a tendency to develop rickets, asymmetrical cranium, keratitis, senile aspect, delayed dentition and reduction in body size and lack of intellectual development, chronic ear disease, neuroses and inherent constitutional debility. That all of these can and do occur in inherited lues of the third generation, I am perfectly willing to admit, but I am not willing to admit that they occur as frequently and to the extent mentioned by the French writer. It is possible, that when syphilis was more virulent, as it undoubtedly was in former times, these signs were more common; but it is quite certain, as any syphilologist or pediatrist now knows, they are at present by no means frequent.

Lemonnier reported a case in which the grandfather had acquired syphilis and his son had congenital syphilis. The son married a healthy woman and from this union two children were born. One of these when examined was twenty-seven years old. He had slight dystrophies of congenital syphilis and when examined was suffering from a gumma of the nose and of the testicles. As far as could be ascertained he never had acquired syphilis. The second child was twenty-four years of age when examined. He showed no hereditary evidences of the disease and denied ever having contracted it. He had ulcerating gummata on both legs.

Pospelow reported a case in which the grandfather was syphilitic, the son had congenital syphilis. He married a healthy woman, who bore him 10 children of whom 8 survived. Seven of these showed no evidences of hereditary lues, but 1 had Hutchinson's teeth and perforation of the nasal septum, and when seen had a syphilitic ulceration of the soft palate.

Chirivino relates a case in which both paternal and maternal grandmothers had acquired syphilis. The father and mother were both congenital syphilitics. One child was born to them which had hydrocephalus and also plantar and palmar syphilides.

Pospelow in a series of autopsies, in which the parents and grand-

parents were syphilitic, states that such infants differ very much from those in which the evidences of simple congenital syphilis, as it is generally understood, are found. The organs and tissues of these infants show a general atrophy, as it were, which is quite distinctive. Many of them, he noted, died without apparent cause. He further states that abortion and miscarriage are not as frequently met with as in syphilis of the second generation and as such are not of the same pathognomonic import as when occurring in the second generation. These infants in the first six months of life are often apparently healthy, many indeed do not show any evidences of the disease until they are five or six years of age. Then without any known cause they waste, and their intellectual faculties become stationary. If they live, they are always far below the normal child. Very few reach adolescence but die usually from some intercurrent affection which may mask the syphilis.

The late R. W. Taylor in 1906 placed on record two cases, which are valuable evidence as to the transmission of syphilis to the third generation. The first case presents the grandmother who contracted syphilis in 1869. She later had secondary and tertiary lesions of marked severity. She represents the first generation. In 1872 this woman gave birth to a female infant which presented typical evidences of congenital lues. This child which represents the second generation seemingly overcame the disease and grew up to be a strong and healthy woman. So far as known she had never been infected with acquired syphilis. In 1890 this young woman, then eighteen years of age, gave birth to a puny female infant. From birth it was marasmic and of low vitality, but aside from this showed no distinct evidences of congenital syphilis. Before it was five years old, however, it developed keratitis, Hutchinson's teeth, osseous swellings, and, later, gummata which broke down in ulcers. In 1905, this child was still alive but suffering from infantilism and general atrophy.

Taylor's second case was that of a healthy woman who married a man who had contracted syphilis two years previously. Two years after marriage, coincidentally with pregnancy, she contracted the disease. She gave birth to a male infant that shortly after birth showed signs of the disease. These evidences persisted until the infant was two years old. He grew up and married a healthy woman. Three years later she gave birth to a weakly female infant. Four years later this infant presented dystrophies of the bones and joints which Taylor cured with active antisyphilitic treatment. This case illustrates extremely well the development of syphilis in three generations. In the first, there was active acquired syphilis; in the second, active hereditary syphilis; in the third, a dyscrasia attended with characteristic syphilitic dystrophies.

While these examples point very strongly to the transmission of the disease to the third generation, the rift in the evidence is the possibility of infection with acquired syphilis in the second generation. In order to prove syphilis in the third generation it is necessary to demonstrate beyond cavil of a doubt that the infant or child representing the third generation has syphilis, as evidenced by the presence of syphilitic lesions or by dystrophies of a syphilitic character, and lastly, in accord with modern methods, that the blood reacts positively to the Wassermann reaction. It must further be proved beyond all doubt that the infant or child is not suffering from acquired syphilis. It must also be proved that the mother or father of the child was suffering from congenital syphilis, and acquired syphilis in either or both must be absolutely excluded. Then it must also be proved beyond all shadow of a doubt that one or both of the grandparents was really infected with syphilis. If these facts can be firmly established the evidence is complete and the contention that syphilis has been transmitted to the third generation is incontestably proved. There is no doubt in my mind that if it has not already been done it will be in the future.

Binary Syphilis.—Tarnowsky, writing in 1904, denies the transmission of syphilis to the third generation. "Syphilitic heredity," he believes, "descending from the second to the third generation manifests itself exclusively by a dystrophic influence." He believes that the apparent transmission of syphilis to the third generation occurs "when a representative of the second generation marries a subject with acquired syphilis." To this combined infection he gives the name of "binary syphilis." He considers that it has a far more noxious influence on the third generation than syphilis of the first generation has on the second. "There are," he goes on to state, "a greater number of abortions, still-births and early deaths, and the proportion of hereditary syphilitic phenomena and dystrophies is increased. Binary syphilis is one of the chief causes of the rapid degeneration of the population of country districts."

It is quite possible that Tarnowsky has given the correct interpretation of syphilis of the third generation. The inability to rule out acquired syphilis in the cases reported by the older authors in the second generation has always been the weak link in their chain of evidence. It was not until 1906 that the Wassermann reaction came into use; and before that mistakes in diagnosis, except by the absence of clinical evidence, which as we now know is no evidence at all, against acquired syphilis must have been frequent. As I have already stated, the future alone will determine the question.

McDonagh is of the opinion that syphilis of the third generation can occur, although it is extremely rare. He has encountered two instances, one of which he has thought worthy of record.

A woman, aged thirty-seven years, brought to him 2 of her children suffering from ringworm. The woman showed evidences of an old bilateral interstitial keratitis, fissures at the angles of the mouth and well marked Hutchinson's teeth. She had given birth to 7 children and had no miscarriages or abortions. He examined the 7 children and found that 2 only had any symptoms of congenital syphilis; the others were perfectly healthy. These 2 children died later at the ages of eight and nine years, of degenerative encephalitis, while the others remained perfectly healthy, but were extremely backward at school. The mother's Wassermann reaction was positive, the father's was negative; the 2 affected children gave a positive reaction, 2 of the others gave a doubtful reaction, which two years later became negative; the other 3 gave a negative reaction throughout.

This is a modern case, as it were, determined by modern methods, *i. e.*, the Wassermann reaction, and in my opinion goes far to establish the authenticity of the facts observed by McDonagh as to syphilis being present in the two children representing the third generation in the incidence of the disease.

The examples given here, all of which are by recognized authorities and verified as far as possible by them, indicate to my mind that syphilis undoubtedly is transmitted to the third generation. Those cases in which the disease shows as active lesions are undoubtedly rare. Those in which it shows as dystrophic degenerations are much more common—more common in my opinion than is generally believed. As Hayes Agnew said many years ago, "Syphilis is the father, congenital syphilis the child, and consumption the grandchild." His words are true. I go on record as firmly convinced that nearly all, if not quite all, congenital dystrophies and inherent weaknesses can be traced to syphilis more or less remote. This may seem a strong statement; nevertheless, I believe it to be true.

Researches made by Neisser and others on the Treponema pallidum tend to show that from the pathologic standpoint the transmission of active syphilis to the third generation is possible. This has been shown by Neisser, in that the organs of heredosyphilitics, including the ovaries, give positive results when inoculated in monkeys. Neisser also obtained positive results from inoculation of monkeys with material obtained from gummata in the tenth and seventeenth years of syphilis. Levaditi also found the organism of syphilis in the ova of heredosyphilitic infants. It has also been demonstrated that the Treponemata pallida are present even in late congenital syphilitics, showing their extraordinary vitality. It is quite possible that the Treponema pallidum remains in the ovum in the latent stage and becomes active after fertilization.

CHAPTER XXIV.

SYPHILIS AND SURGERY.

Text-books on Surgery.—The text-books on surgery—large and small, old and new—usually devote a chapter or section to syphilis. The importance of the subject warrants this; but all of these volumes of surgical lore treat the subject in the traditional way. That is, they give a brief account of the pathology, the symptoms and treatment of syphilis. Not one of them discusses lues from the standpoint of surgical pathology or diagnosis; not one of them refers to the influence of the disease upon surgical conditions in detail or as a whole.

In my opinion this is wrong. It is an inexcusable omission. For, as every surgeon as well as every syphilologist well knows, syphilis exerts a profound influence upon many conditions which are strictly surgical; and it also, in many instances, gives rise to conditions which can no longer (because of their nature) come under the direction of the syphilologist but pass to that of the operating surgeon.

In another chapter I have discussed syphilis and malignancy, and I believe I have shown the relation that exists, more or less, in regard to syphilis as a causative factor, a modifying factor and as a problem in differential diagnosis. But malignancy is not the only surgical problem in which syphilis is often mightily concerned. There are others, and these I will here discuss. It is in this light, therefore, that I consider syphilis in its relation to surgery.

Syphilis and Prognosis.—The surgeon, more so perhaps than the internist, is called upon to render an accurate prognosis. This is expected of him because his work is in a way more mechanical than is non-surgical treatment. It is necessary for him to know not only when syphilis is present in a patient about to undergo a surgical operation, but also in what way the luetic disease will change or modify his prognosis of the ultimate result. Lack of this knowledge may lead him into grave errors from which he may have much difficulty in extricating himself.

Syphilis and Surgical Operations.—Syphilis, inherited or acquired, is always a possible injuriously modifying factor in any surgical operation. By this I do not mean to assume that every surgical operation on a patient with a positive Wassermann or other evi-

dences of present syphilis will not respond to that operation or that the condition requiring surgical interference, whatever it may be, is due in every instance to the syphilitic infection. I will quote the words of Martin apropos of this: "There are in hospitals at this moment thousands of patients perishing from the corrupting influence of a positive Wassermann upon the mind of the surgeon; drained by the steady progression of a condition which called for prompt surgical relief, and even more actively sapped by the long-continued and futile administration of mercury, arsenic and iodide of potassium."

Wassermann Reaction not a Contraindication to Surgical Procedures.—There is no doubt in my mind that many patients suffer for the want of a surgical operation because the surgeon is blinded by the presence of a positive Wassermann. Nevertheless, no operation *per se* is free from the deleterious influence of the disease. This statement may be said to carry the weight of an aphorism. It may not be as ancient as some of those of Hippocrates but it is just as true. There is no doubt, as every experienced surgeon well knows, that many good operative procedures have resulted disastrously because proper antisyphilitic treatment was not administered either before or after operation.

Antisyphilitic Treatment Needed in Surgical Cases.—Except in emergencies no operation should be performed while the patient is suffering from the primary stage, or more particularly the secondary stage of the disease. The reason for this is that in the florid stage of syphilis the chances of primary union are much jeopardized. The wound often fails to heal with the promptness which it is natural to expect under aseptic methods. Instead of a clean-cut scar, pale, flabby granulations form; the stitches cut through, and not infrequently when the stitches are removed the wound gapes as widely as when it was first made. This of course should not be. Yet it not infrequently occurs, and this, too, in the practice of men of skill and experience who have neglected the precautions I have mentioned. In so far as tertiary syphilis is concerned the danger is not so great, except that the lesion to be operated upon may give rise to an error of diagnosis; yet tertiary syphilis may be, and not infrequently is, a cause of delayed union in an operative wound. It is the part of wisdom, therefore, wherever syphilis is present in a patient about to be operated upon, to fortify him, as it were, with antisyphilitic treatment, preferably before the operation is to be performed if time will so allow. Otherwise, treatment should be instituted as soon after the operation as possible; that is, within four or five days after if ether has been given in order not to put too much stress upon the kidneys, as ether is eliminated largely through the kidneys, just as arsphenamine and mercury are.

Granuloma of the Tongue.—There are certain conditions which when arising from causes other than syphilis may be regarded as surgical, but when due to syphilis require surgical interference comparatively rarely. Amongst these may be mentioned circumscribed granuloma of the tongue. At the onset this is almost invariably syphilitic and if so diagnosed can be treated in the usual way which causes it to disappear rapidly and completely. If untreated, however, it nearly always goes on to carcinomatous transformation and we then have two conditions existing simultaneously, viz.: syphilis and carcinoma. In this event the surgeon will be confronted with a positive Wassermann and a growth that to all intents and purpose is malignant. He will necessarily operate and at the same time administer antiluetic treatment.

Gummata and Myomata.—In tertiary syphilis myomata of the voluntary muscles are not uncommon. These tumors usually can be felt very distinctly imbedded in the belly of the muscle. Often, however, instead of these tumors there is a gummatous infiltration. Frequently the two conditions occur in combination. One or many muscles may be involved. When gummatous infiltration occurs it takes place very slowly. There is little or no pain, but after a while the patient notices that he cannot bend his arm or leg as the case may be. There is a seeming increase in the size of the muscle and it also becomes shorter. The tendons stand out sharply even when the muscle is not contracted. The inflamed muscle may become adherent to the skin and ulceration and sinus formation may take place. These cases can be cured by internal medication, but in those which have been allowed to go on until destructive changes have taken place tenotomy may be required; they thus come under the care of the surgical specialist.

Gangrene. Aneurysm.—The predilection of the treponemata for the vessel walls may sometimes cause an obliterative endarteritis of the vessels supplying a part, and gangrene consequently ensues, I am convinced that this accounts for many of the cases of gangrene arising in the course of diabetes. When trauma can be ruled out, aneurysm is invariably caused by syphilis and treatment has little or no effect upon it. Where it is accessible it should be removed by surgical means. Pressure of syphilitic new growths upon large vessels of the leg or arm which may or may not respond to antiluetic treatment should be removed by the knife if possible. These growths are not infrequently diagnosed as sarcoma. As the difference in the prognosis between sarcoma and syphilis is very great, extreme care should be exercised by the surgeon in making a diagnosis. I may add that, to complete the surgeon's confusion, a patient suffering with sarcoma not infrequently shows a positive Wassermann even when syphilitic disease is not present.

Lymphomatosis.—Syphilis may sometimes cause a generalized lymphomatosis in which the glands are enlarged to a marked degree, so much so that the condition may be confused with Hodgkin's disease. The blood picture and the Wassermann reaction will however clear the diagnosis. Should this glandular enlargement resist internal treatment, as it sometimes does, and should some of the glands press upon nerves or vessels, as in the neck for instance, giving rise to coughing, aphonia and dyspnea, they should be removed by surgical means.

Stricture of Rectum.—Stricture of the rectum is very frequently an end-result of long standing syphilitic inflammation of this portion of the gut. The fibrosis thus resulting is not amenable to antiluetic remedies and here the aid of the surgeon is called in requisition to dilate or resect the constriction.

Syphilis of Testicle.—When syphilis attacks the testicle, either the gland proper or the epididymis, as it not infrequently does in the tertiary stage, it is nearly always amenable to treatment. But if, through neglect, the gummatous mass is allowed to caseate and go on to sinus formation medical treatment is then of no avail and surgical measures must prevail. In some instances syphilis of the testicle takes the form of hydrocele which if recent should be tapped and strapped and antisyphilitic treatment administered. As a rule, however, the condition advances insidiously and is accompanied with considerable thickening of the tunica vaginalis. These cases should be operated upon—the method of Jaboulaye is in my opinion the best—and as soon after the operation as possible, that is when the ether has been completely eliminated, treatment should be given.

Syphilis of Liver.—The researches of Warthin and others have proved conclusively that the Treponemata pallida often have a nidus in the liver where they may harmlessly exist for many years. Should they be aroused to activity from any cause, grave hepatic disturbance may result. In some instances of gummata of the liver they take the form of projecting and prominent masses which may be mistaken for malignant disease. Frequently in conjunction with them adhesions form which may give rise to a variety of symptoms. Usually these syphilitic new growths respond rapidly to medication and quickly disappear. But this is not always so with the adhesions remaining. These may require surgical interference.

Tumors of Mediastinum.—Tumors of the mediastinum are sometimes caused by syphilis. When such is suspected or diagnosed a Wassermann should always be taken and, if positive, treatment instituted at once. Such a case has been reported by Dittrich occurring in a girl, aged sixteen years; it was first thought to be a malignant lymphoma but it quickly disappeared under the influence of mercury.

Tumors of Bladder.—Syphilitic tumors of the bladder have been reported but they are perhaps the rarest of all syphilitic new growths. Clinically they present no features to differentiate them from tumors arising from other causes. They are rarely if ever pedunculated; and this is about all that can be said concerning them from the standpoint of differential diagnosis. When these growths are encountered it should be remembered that it is possible, although not probable, that they may be syphilitic.

Ulcer of Stomach.—Syphilis sometimes, although rather rarely, may attack in the tertiary stage the gastric mucosa and cause a typical ulcer of the same with the usual symptoms pertaining thereto. Treatment will usually cause the lesion to disappear but surgical measures may be required especially if contracture occur as in the so-called "leather bottle stomach." McNeil operated for what he thought to be cancer of the pylorus but which he found to be an annular constriction due to lues. He resected the pylorus and the patient recovered. Easterman reported in 1917, 23 cases of syphilis of the stomach from the Mayo Clinic. Of these, 10 were operated upon and 13 were not. Of the cases operated upon, 2 were lost track of, and of the remaining 8, 3 were cured and 5 much improved. All received antisyphilitic treatment in conjunction with the operative procedures. Easterman brings out the following facts: The diagnosis was made by the Wassermann reaction and the *x*-ray. The symptoms strongly suggested gastric ulcer, but the examination of the stomach contents was suggestive of carcinoma. The lesions were found to be gummata, usually multiple, and accompanied with a considerable degree of diffuse infiltration. There was also noted variable degrees of contracture with thickening of the stomach wall, giving rise to more or less deformity and perigastric adhesions, which in most instances involved the pyloric segment, (*vide* McNeil's case). It will thus be observed that such eminent surgeons as the Mayo brothers sometimes deem it expedient to operate in gastric syphilis or rather the results thereof. For it is mostly in those cases, where fibrous sequelæ have followed active lesions, that surgical interference is required.

Cerebral Tumors.—Syphilitic gummata which do not respond to treatment comprise from 5 to 8 per cent of cerebral tumors. If these tumors are accessible it is justifiable to remove them. If they are inaccessible a decompressive operation is advisable. An important symptom in these cases is choked disk. Intraventricular and intraspinous medication has in my opinion greatly lessened the necessity for surgical interference in many of these cases. However the removal of these new growths—for such they are—if unresponsive to treatment, is a perfectly logical procedure and is fraught

with comparatively small risk as the number of successful cases recorded plainly shows.

Necrotic Bone.—In the days of Ricord, a syphilitic sequestrum of bone, especially of any of the bones of the face, was let severely alone, because of the fear of erysipelas. This fear, which in those days was an ever present one, exists no longer. If a piece of necrotic bone separates or is loose, we need only to inject a local anesthetic and remove it. When this happens to the nasal bones it may be necessary to split the nose in order to remove the multiple sequestra present. Pozzi makes an incision in the median line and applies the white hot cautery to all suspicious depressions in the fossæ and sinuses. The Volkmann spoon is used by some for this purpose. In repairing the damage caused by necrosis of the nasal bones, it is advisable to wait until the active symptoms of the disease have subsided under the influence of treatment, otherwise good cicatrices cannot be obtained. Rouge, Ollier and others have practised typical operations to correct the deformities of cicatricial contractions within the nose. Konig and Nelaton have combined internal and external plastic work in order to reconstruct an efficient and cosmetic organ. Others have employed prosthetic devices to replace the destroyed bone. Naturally this comes under ordinary rhinoplasty which has a field in correcting the results of intranasal syphilis.

Nasal Bones.—The sequestra which occur in tertiary syphilis of the nasal bones is due to pyogenic organisms. Antisyphilitic treatment while it soon conquers the spirochetal invasion is powerless against the suppurative process; for that reason these sequestra require removal, and plastic surgery is called in to aid in correcting the deformity caused thereby. These cases are sometimes complicated by sinus emphysema, in which event the usual surgical methods are employed along with constitutional treatment.

Mouth and Jaw.—The surgery of tertiary lesions of the buccal cavity includes the curettement of broken down gummata and the removal of sequestra from the jaw and the use of prosthetic devices to close defects so caused.

Larynx and Pharynx.—The larynx is not infrequently the site of attack of tertiary syphilis. In their active stage these lesions are usually accompanied by suppuration. The actual lesion is either a chrondritis or a perichondritis. Because of the pus formation they sometimes require to be incised and drained. Edema of the glottis occasionally occurs in these cases, when an emergency tracheotomy may have to be done. As an end-result of tertiary syphilis of the pharynx stenosis sometimes occurs. The narrowing of the aperature may require the use of bougies or the division of the cicatricial bands with the knife.

Periostitis.—Syphilis in the tertiary stage attacks the bones with great frequency. None are exempt. The luetic process may assume either of three forms or they may be combined in their attack. The covering of the bone—the periosteum—alone may be affected and this may be either localized or diffuse. Syphilitic periostitis is most often seen in late hereditary syphilis although it is by no means uncommon in the acquired disease. Periostitis due to syphilis is almost invariably excited by some slight trauma. It begins as a painful swelling over the bone, attached thereto but gradually shading off until it cannot be told where it ends. The skin is movable over the swelling and may be only slightly reddened or not at all. Should the trauma, slight as it may be, be repeated or if the patient is in a debilitated condition, suppuration may take place and as the pus approaches the surface a funnel-shaped ulcer is formed.

Instead of being strictly localized the periostitis may be diffuse. This causes a decided increase in the size of the bone. The swelling is hard and as a rule is painless and there is no impairment in the use of the limb should it be one of the long bones that is attacked. This proliferation of new bone may later harden and cause a permanent increase in the size of the bone. The bone produced by this periosteal inflammation, on the other hand, may separate and the space between become filled with broken down caseating material. Not infrequently these cases are mistaken for sarcoma. The *x*-ray will show the difference, however, as the syphilitic inflammation involves the whole circumference of the bone, whereas in sarcoma the growth springs only from one side.

Osteitis.—The syphilitic inflammation may attack the bone as a local or a diffuse osteitis. It may or may not be accompanied by periostitis. This osteitis causes an obliteration of the cancellous tissue and a consequent sclerosis which makes the bone larger and heavier than its fellow. Occurring as it usually does in the femur or tibia the patient will limp, and complain of pain. The condition may be diagnosed as rheumatism or tuberculous disease. Should this localized gummatous osteitis occur in a condyle of the femur or the humerus it may also be accompanied by a gummatous synovitis. Here we have pain, limitation of movement and swelling, so that it is not infrequently diagnosed as tuberculosis. A distinguishing sign, however, of very great importance is that in the syphilitic disease there is no wasting of the muscles, and the pain while present is by no means as severe as in tuberculous disease.

Cranial Bones.—Tertiary syphilis in the forms mentioned not infrequently attacks the bones of the cranium. Should a mixed infection occur sequestra form and if the pus shows a tendency to

burrow the danger of meningitis is very great. The removal of these sequestra of the calvarium should not be precipitate for fear of the possibility of meningitis already mentioned. Their removal should not be undertaken until it can be accomplished with the least possible force. In very many instances, even when a piece of bone of considerable size has come away, it not infrequently happens that the gap is filled in with new bone. Any surgical procedure in this locality should always be preceded by vigorous antisyphilitic treatment. Periostitis or osteitis of the cranial bones does not always terminate in sequestra formation. In many instances the active process declines and eburnation of the proliferated bony tissue takes place leaving large bosses on the skull. These prominences are sometimes so large as to be actually disfiguring. In such instances they may be removed by the burr or chisel.

Syphilis of Joints.—Operative surgery plays a very minor role in syphilis of the joints, quite the contrary to its part in tuberculous disease. In the secondary stage there is sometimes to be noted a rapid serous effusion into one or more joints—usually the knee. It is attended by considerable pain but the pain is not increased by movement. The skin over the joint may be slightly reddened. Palpation reveals some thickening of the perisynovial tissues. Crepitation is not present. The swelling disappears as rapidly as it comes and as it leaves one joint it may appear in another, or several joints may be affected simultaneously. This condition is not infrequently mistaken for rheumatism.

Synovitis.—Chronic syphilitic synovitis comes on very insidiously. It is more frequent in women than in men and the knees are the joints most frequently affected. There are no inflammatory changes to be noted except the swelling. The pain is slight or it may be entirely absent. The motion of the joint is hardly interfered with and there is no wasting. This condition also is frequently mistaken for arthritis of rheumatic origin.

Gummatous Infiltration of Joints.—In the tertiary stage of the disease gummatous infiltration of the joint not infrequently occurs. It affects either the articular ends of the bones forming the joint or the synovial membrane. It is usually accompanied with other evidences of syphilis elsewhere, such as gummata of the skin, rupia or other lesions.

The condition is of slow onset, the joint gradually becoming uniformly enlarged although the patient can move the limb easily. There is no wasting of the muscles above or below the joint, nor is there any displacement of the articular ends of the bones. The synovial membrane is much thickened but there is not much increase in the fluid contents of the joint. The gummata can often be felt

as isolated masses in the thickened synovial membrane. When the articular ends of the bones forming the joint are affected the swelling about the joint assumes a globular shape due to the proliferation of bone. The synovial membrane may not be thickened, and there is not much increase in the amount of fluid in the joint. Pain is often absent although the patient may complain of osteocopic pains. Sometimes, however, the pain may be severe. The knee and the elbow are the joints most often affected. In some instances instead of a slow onset the process may be very rapid and unless promptly checked by energetic treatment the joint may be destroyed. In these latter cases fistulous tracts discharging caseating material will form, and later the joint may either become ankylosed or the articular ends may become eroded and a flail joint results.

Syphilis and Tuberculosis of Joints.—Tertiary syphilis of the joints is, as is natural to suppose, most frequently mistaken for tuberculous disease. In many instances it is my opinion that the two infections are commingled, as it were, in the affected joint. There are certain points of difference, however, which will generally aid in making a diagnosis. In syphilitic disease there is usually little pain. Tuberculous disease is attended with much pain—it is a characteristic feature. In tuberculous disease there is always wasting about the joint, which rarely happens in syphilis. In tuberculous disease the movement of the joint is impaired at an early stage. In syphilitic disease it is not until the termination of the process that the power to use the joint is completely lost. Again there may be evidences of syphilis elsewhere which allow of diagnosis, and the same is true of tuberculous disease.

In some instances, when suppuration is present, these syphilitic joints may require to be opened and drained. In the flail, or "Charcot's joint," surgical interference is of no avail. Mechanical devices will sometimes afford a certain measure of relief. Should the surgeon decide upon resection of the joint vigorous treatment should be instituted as soon after the operation as possible in order that union of the severed ends may take place. As a rule tertiary syphilis attacking the bones, if diagnosed early, will nearly always yield to treatment. It is in those cases where the damage has already been done that the aid of the surgeon is required.

Sabre Tibia.—The so-called "sabre tibia" sometimes seen both in hereditary and acquired syphilis may be chiseled straight for cosmetic reasons. Periosteal inflammation is rarely the cause of sequestra. The bone becomes carious instead. It may be necessary to chisel out this carious bone which will fill either by fibrosis or the formation of new bone.

Clavicle.—A bone that is frequently attacked by the Treponema pallidum is the clavicle, the external end being the usual point of

selection for the disease process. It shows gummatous prominences, or tophi, which later breaks down, and if infected by pyogenic organisms promptly suppurate. These lesions grow very rapidly—so rapidly in fact that they are frequently mistaken for sarcoma. The treatment (owing to the rapid destruction) is surgical, a total or partial excision of the bone being necessary.

Fractures.—Contrary to current opinion syphilis attacking the shaft of a bone rarely causes fracture. The rare condition known as *fragilitas ossium*, in which the bones break very easily—the so-called pathologic fracture—is not caused by syphilis. While the condition can occur in a syphilitic, it is not *per se* due to the luetic disease. The 15 cases of syphilitic fracture, collected by Gurlts, are in my opinion open to doubt in so far as syphilis is concerned. However, I do not mean to infer that an osseous inflammation originating from syphilis cannot and does not cause pathologic fractures. On the contrary, I am convinced that it sometimes does. What I mean to infer is that it occurs from syphilis with comparative infrequency. This is shown by the fact that after an extensive search in the literature I have found only 50 cases recorded. When we consider the wide incidence of the disease this is a very meager showing, and I am justified in saying that it is of very rare occurrence. In the cases recorded the number of fractures exceeds the number of individuals affected. It is therefore natural to infer that these fractures are more apt to be multiple than single. None of these fractures has been recorded as occurring before the sixth year of the disease. It must be considered therefore as a symptom of late occurrence—that is of a strictly tertiary character. In most of the cases pain was absent and, in this, syphilitic fracture differs from *fragilitas ossium* in which the fracture is always preceded by pain. However, cases are included in which pain was present in the syphilitic form. The humerus, femur, clavicle, radius, tibia, ribs and patella were the bones fractured; their frequency occurring in the order named. The pathologic fractures which sometimes occur in infants with hereditary syphilis are in many instances a separation of the epiphysis from the shaft owing to faulty union caused by the disease. While syphilitic fractures may be regarded as true pathologic fractures it will always be found that the immediate cause was some slight trauma. This is explained by the fact that the bone is weakened by the process of the disease; yet if no stress is put upon it, the bone will still remain whole because of the support given to it by the surrounding tissues. Now a trauma, even if slight, where the bone is much weakened, is enough to destroy, as it were, this stability and consequently the fracture occurs. For instances, a bone may be so eaten away that only a slight spicule unites the two parts like a narrow isthmus of bone

as it were. It is easy to understand how a trauma such as a very slight blow or knock will break this and thus separate the two ends of the bone.

Traumatic Injuries.—These are frequently influenced by syphilis. It is also true that trauma occurring in a syphilitic is often the beginning of a syphilitic process. This is exemplified by the fact that head injuries may precipitate paresis or some other form of cerebral syphilis. Trauma may originate an aneurysm; or a foreign body lodged in the eye of a syphilitic may cause an iritis. Irritation on the site of a healed cutaneous gumma may cause it to renew its activity. Cases of this kind have been cited by Klauder and others. While syphilis *per se* may not be a cause of fracture yet fractures occurring in a syphilitic frequently do not unite or unite only after a long period or by fibrous union. For that reason any fracture in which union is delayed or is fibrotic should arouse suspicion of syphilis, and a Wassermann test of the serum should be made as well as a roentgen-ray examination of the lesion. Bursitis occurring after prolonged irritation such as would be caused by kneeling or pressing with the knee may be due to the syphilitic dyscrasia. This fact has been brought out by Verneuil, and the presence of such a condition should always cause an inquiry as to the existence of syphilis.

Not infrequently syphilis is not suspected in many of these traumatic injuries which fail to heal. The patient may not know that he has the disease, or he may think that he has been cured, or the former existence of a chancre may not to his mind be of sufficient import to bring to the attention of the surgeon. Knowing the influence that syphilis may exert upon any traumatic lesion it is the part of wisdom to search for it in every instance. By so doing much will be gained in many instances.

Surgery of Syphilis.—Tertiary syphilis attacking the soft structures or the bones may appear at first glance most threatening, and so it is unless its progress is promptly stopped. But since we are dealing with a strictly constitutional disease caused by a specific organism, which may be said to permeate every tissue of the body, surgery which can offer only local aid is of no avail. Surgery in syphilis is of aid therefore only in correcting the end-results of this process after it has ceased its activity. In other words, surgery can help the sequelæ but not the disease. Surgery is concerned with syphilis in diagnosis rather than in operative procedures.

CHAPTER XXV.

SYPHILIS AND GYNECOLOGY.

Syphilis in Women.—It is usually more difficult to diagnose syphilis in women than it is in men. I desire to go on record also as being of the opinion that syphilis is not as a rule so severe in women as it is in men. In so far as neurosyphilis is concerned it is certainly much less frequently encountered in females than it is in males. This is strange because the nervous system in females is more sensitive and highly organized than it is in men. It is difficult to give a reason why women are more lightly affected with the disease than men. It has been said that it is because lymphocytosis is greater in women than in men; also because the thyroid gland is more active and secretes a greater amount of iodine which consequently acts as a physiologic alterative, as it were. Both of these reasons may be correct and probably to a certain extent have some influence in modifying the symptoms of the disease as seen in females. That they are the only reasons, in the state of our present knowledge, I do not pretend to say.

Chancre.—There are a number of reasons why syphilis is more difficult to diagnose clinically in women than in men. In so far as the primary sore is concerned this is because of the conformation of the external genital organs. Many women, as every gynecologist and syphilologist knows, are not aware of having had a chancre, and when it is present they suffer little or no discomfort from its presence. In fact, in the female, when occurring on the genitals, the chancre is often very small and ephemeral in character. In females in very many instances the chancre lacks the characteristic induration which is an almost invariable concomitant of chancre when it occurs on the penis.

The Vulva.—In searching for chancre in a female let us consider the vulva as composed of three planes—(1) a superficial, in front of the mons Veneris and behind the labia majora; (2) a middle, consisting of the labia minora and the clitoris; and (3) a deep, consisting of the vestibule, meatus urinarius and the vaginal orifice.

Chancre.—These cover one another so closely, especially in multiparæ, that they seem to be composed of one body and because of this configuration present the principal difficulty for exposing for diagnostic purposes the initial lesion of the disease. The

chancre may be situated on the labia majora, in which event the perception of the sore is easy; but this is not the most common site of the lesion. Frequently it is hidden in the fold that lies between the vaginal lips and under the hood of the clitoris close to the meatus urinarius or behind the labia minora, especially when these are large and prominently projecting. Or, the chancre may be found behind the fourchette or in a fold in proximity to the carunculæ myrtiformes. Or, the chancre may be on the cervix uteri. This last is an extremely rare site but occasionally it is found there.

Induration is a characteristic of chancre occurring on the penis of males; in females the chancre is rather of a parchment-like consistency and for this reason often escapes discovery. The reason for this lack of induration in women is because the condition does not, as some suppose, depend upon the nature of the ulceration itself but upon the structure of the parts beneath. Any inflammatory neoplasm will therefore be all the harder the more difficult it is for the inflammation to spread. For example, the hard chancre is most frequently found in the male in the balano-preputial groove, because here it lies upon the elastic fibers which constitute the larger part of the glans. In the female the chancre is found mostly on the labia majora or labia minora or in the fourchette, just where by reason of the nature of the underlying tissues, induration could not occur.

Diagnosis of Chancre.—Chancre occurring on the vulva is sometimes extremely difficult to diagnose from simple herpes which is nearly always present in some women. It may have to be distinguished from a slight abrasion due to coitus or some other cause. As to chancroid it is usually so typical and gives rise to so much pain and discomfort that it is comparatively easy to diagnose between it and chancre. In not a few instances, chancre is accompanied by edema and should any edematous condition of the parts be found it is wise to make a painstaking search for chancre. A most important concomitant in chancre, and one which should not be overlooked, is adenitis. The words of Ricord are true when he says: "Adenitis folllows a chancre as the shadow the body." This adenitis is almost always on the same side as that upon which the chancre appears. The glands are not painful, which is invariably the case in chancroid, but are distinct and hard and can be felt like beans, separate and distinct beneath the skin. In ulcerated herpes there is no adenitis; and in vulvitis if accompanied with adenitis it is invariably bilateral.

Secondary Syphilis.—When we consider the secondary symptoms of syphilis as occurring in women diagnosis is not so difficult; but here we also encounter difficulties which are not usually present in men. In women the roseola may be so slight, so fleeting and

ephemeral that it comes and goes unnoticed. A hot bath in these cases will sometimes cause it to appear more pronounced. Some women have a skin of a peculiar mottled color which may simulate a roseola very closely and also disguise it when it is present.

Pigmentation.—In the more advanced stage of the disease there is a sign of the disease which is very frequent in women and only rarely met with in men; this is the so-called pigmentary syphilide of the neck. This pigmentation is really only an exaggeration of the natural pigmentary elements of the skin. It not infrequently takes a lace-like form, that is, it shows little islands of pigmentation interspersed with clear spaces. This pigmentary collar is, I might say, almost pathognomonic of syphilis in women. It may be the only sign or it may be accompanied with other evidences but if it is present, the disease can nearly always be proven by some other evidence if sufficient search is made.

In women it is often difficult to obtain definite facts as to when infection occurred and also as to the evolution of the disease unless these have been of a very obvious character. For this reason when syphilis is suspected in a female a very careful clinical examination is necessary—this, aside from the taking of a Wassermann. In women it has been my experience that the Wassermann is often aberrant, *i. e.*, it is in very many instances apt to be paradoxical as it were. The clinical signs may be very patent and yet the Wassermann will show negative and again the Wassermann may be positive and no sign or history of the disease can be obtained. This statement will, I know, be contested by some, nevertheless I have found it true in a sufficient number of cases to warrant it being taken into consideration.

Frequency in Women.—It has been said that syphilis is more common in men than in women. Recent observations by competent observers based upon histories and Wassermann tests seems to show that syphilitic infection is higher in women than in men. My own experience has been that syphilis is much more frequent in women than is generally supposed. A surprising number of women will give positive Wassermann reactions in whom syphilis has never been suspected either by themselves or their medical attendant. It is undoubtedly true that many functional disturbances in women supposedly due to derangements of the genital organs are due to an unsuspected luetic infection. It is the part of widsom, therefore, to take the Wassermann of every woman complaining of some vague disturbance as well as of those who are pregnant. In the pregnant woman a Wassermann should invariably be taken to safeguard both the mother and her unborn child. When this is done promptly much valuable time is often saved in the treatment of the disease should it be found present.

Women seem to enjoy a relative immunity to the Treponema pallidum and the disease as a whole pursues a much milder course than in men; for example about 9 per cent of women infected with syphilis have secondaries so mild that they are not aware of their existence. In the secondary stage of the disease, however, women are peculiarly liable to a general toxemia which may be very severe and at the same time may show very few if any of the characteristic lesions of the second stage of the disease. This toxic fever of luetic origin occurring in women is sometimes mistaken for malaria or typhoid which it simulates with comparative closeness. If a correct diagnosis is not made the symptoms after a time gradually abate and it may be years after when a tertiary outbreak occurs that the continued fever which has been ascribed to some other cause is known to have been of syphilitic origin.

Infectivity.—There is ample evidence to believe that women who have not received treatment remain infective for years although they may show absolutely no clinical signs of the disease. Especially is this true of women in regard to infecting the fetus. This power to infect the fetus may persist while infectivity in other respects is in abeyance. For this reason, as sometimes occurs, a woman infected by her first husband may bear syphilitic children by her second husband although the latter does not contract the disease from her.

Chancre d'emblée.—It is with women that chancre d'emblée most frequently occurs. In men it is rarely found. With women, I share the opinion of Gaucher, that it happens more frequently than is usually supposed. A chancre can occur only on the cutaneous surface or a dermo-papillary mucosa, that is, a surface which is covered with pavement epithelium, such as the buccal or pharyngeal mucosa, or the nostrils, the anus beneath the sinus line of Morgagni, the semimucous surface surrounding the anal orifice, the vagina and the cervix uteri. Syphilis not inoculated on a mucous surface of pavement epithelium cannot begin as a chancre. If during coitus the Treponema pallidum penetrates with the semen into the uterus instead of lodging on the vulval surface, the vagina or the cervix uteri, the organisms are absorbed through the mucous lining of the uterus and thence become generalized throughout the system without the formation of a chancre. This is syphilis d'emblée or syphilis without a chancre.

Initial Secondary Syphilis.—The intra-uterine absorption of the Treponema pallidum causes an initial secondary syphilis, if I may be allowed to use such a term; or, perhaps, it would be better to say that a secondary syphilis immediately arises without a primary lesion.

The skin and dermo-papillary mucous membranes, the superficial

surfaces of which are composed of pavement epithelium, are unable to absorb liquids, and inoculation upon these surfaces can only take place through a solution of their continuity. Mucous surfaces, which are lined with cylindrical epithelium, are able to absorb fluids and through such a surface the infective agent can gain access to the body without a break in their surfaces. It is thus that syphilis d'emblée occurs in women with comparative frequency.

Slow Syphilization.—It has been observed that tertiary syphilis existing in the husband and which is not directly infectious by reason of the total absence of lesions, can still infect the woman by means of the semen entering the uterine cavity and this too without the woman being pregnant. It is to be understood however in this connection that if fecundation takes place the woman is infected during the process of conception, but intermediately through the fetus. In these cases it may be said that the transmission of the disease does not always take place in an active way. It may be termed a slow process of syphilization, as it were, in which by a slow and insidious process syphilization takes place and this syphilization may remain dormant indefinitely and can only be discovered by means of the Wassermann reaction.

Secondary and Tertiary Lesions.—The secondary and tertiary lesions of syphilis of the external genitals in women include the mucous patch and the gumma. The rare condition known as ésthiomène or syphiloma vulvæ I will discuss in another chapter. These lesions have the same general characteristics as when they appear in other parts of the body. Flat condylomata are not infrequent and may also invade the region of the anal orifice. If the woman is fat they may give off a disgusting odor. These lesions may be associated with more or less edema of the parts and the ulceration is sometimes extensive. They may have to be differentiated from tuberculosis, elephantiasis and ésthiomène. The diagnosis in doubtful cases can nearly always be made by the discovery of the Treponema pallidum and the Wassermann reaction.

Tertiary Lesions.—Tertiary syphilis of the vulva and vagina usually presents itself as a persistent and destructive ulceration. When occurring in the vicinity of the vestibule it not infrequently leads to destruction of the urethra unless checked by treatment. These patients are usually women of uncleanly habits and are also in a debilitated state of health, so that their tissues offer but a slight resistance to the disease. Many times the ulceration is further complicated with a pyogenic infection. Many of these cases also have ulceration of the rectum which not infrequently heals with stricture formation. When syphilitic ulceration affects the vaginal fornices and the cervix uteri it is very often mistaken for carcinoma. The Wassermann test and the microscopic findings will clear the

case. Further, they rarely cause pain and when occurring on the cervix do not bleed as freely as is the case with carcinoma. They yield to treatment but often leave disfiguring cicatrices.

Condylomata Lata.—Condylomata lata are frequent manifestations of the disease occurring on the vulva during the first twelve or eighteen months of the disease. They are really moist papules which from their anatomical situation take on the appearance of flat warty growths. They vary much in size, from a pin head to a lima bean. The lesions are usually multiple and in some instances they may coalesce and form one large one. Usually they are not painful unless irritated.

Syphilis of Bladder.—Syphilis of the bladder in females as in males is of extreme rarity. The manifestations are nearly always of the tertiary type and appear as papillomatous elevations or as ulcerations without distinct characteristics. They can be recognized only by the cystoscope and the diagnosis is made only by the Wassermann reaction and by examination of a piece of tissue for Treponema pallidum. This coupled with the fact that they rapidly disappear under antisyphilitic treatment is the only means whereby they can be diagnosed. Gummata of the bladder may show no signs of their presence and may be discovered by accident in the course of cystoscopy. If these neoplasms become ulcerated they may cause hemorrhage, and for that reason hemorrhage from the bladder where tuberculosis or malignancy or hemorrhagic villous growths can be ruled out should arouse suspicion of syphilis.

Syphilis of Uterus.—Syphilis of the internal organs of the female present a number of problems as yet unsolved. Among these is the question whether certain parts of the female genitals possess a relative immunity as it were to the infecting organism of syphilis. Chancre of the cervix presents the best known of syphilitic affections of the internal generative organs of the female. At best, this is comparatively rare. The disease has been known, however, to manifest itself upon the cervix in the form of macules, papules and ulcerations. The macules and papules give rise to no special symptoms and as a rule are only recognized during examination with a speculum. Ulceration of the cervix due to syphilis may cause a profuse leucorrheal discharge. These cervical lesions yield rapidly to treatment and usually leave no trace of their former presence. Our knowledge of syphilitic lesions of the body of the uterus is very meager. There is no record as far as I have been able to find out of any primary or secondary lesions having been found within the body of the uterus. A few instances of gummata occurring in the walls of the uterus have been recorded and an isolated observation by Hoffmann shows the possibility of gummatous infiltration of the endometrium. This frequency of tertiary lesions

would therefore suggest a relative immunity of the uterus to the invasion by the organism of lues.

Fallopian Tubes.—It has been state that the Treponema pallidum has never been found in the tubes of syphilitic women; but I know of no reason for this.

Endometrium.—It is my personal opinion that gummatous infiltration of the endometrium is more common than is usually supposed and that the supposed immunity of the corpus uteri is more apparent than real. The chief symptom of this condition is hemorrhage. It occurs chiefly as a menorrhagia. Where other causes can be ruled out this symptom occurring after thirty years of age should cause syphilis to be considered as a possible disturbing factor.

Ovaries.—Various changes in the ovaries have from time to time been described as typical expressions of the secondary or tertiary stage of the disease. But after careful consideration of the literature I am forced to conclude that as yet we have no positive proof that the luetic factor can be held as the sole determining factor. As this is written the Treponema pallidum has not as yet been demonstrated in the ovaries.

While scientific accuracy demands the examination of all suspected tissue for the determination of the character of the condition, the practitioner who is without laboratory facilities should administer antisyphilitic treatment in any case of uterine hemorrhage when it is not possible to discover any local or constitutional cause for such hemorrhage, such as polyp or carcinoma.

Cervix.—Gaucher recorded a case where multiple chancres of the cervix uteri were mistaken for epithelioma and operated upon for such. Tertiary syphilis of the cervix uteri has received comparatively slight attention both from gynecologists and syphilologists. The literature is inconspicuous and with the exception of a very few monographs, affords very little light upon the subject.

As long ago as 1839, Duparcque observed cervices enlarged and ulcerated which yielded promptly to the antisyphilitic treatment of the day. In 1864, Lancereaux argued that there was ample evidence that tertiary lesions of the cervix occurred as gummata as they do in other viscera attacked in the tertiary stage of the disease. He also called attention to the fact that the apparent rarity of the lesion might be due to confusing it with other lesions of the cervix. In 1874, Henry reported three cases of induration and enlargement of the cervix due to syphilis, which rapidly disappeared under antiluetic treatment. Neumann in 1896 contended that while gummata of the cervix alone were most infrequent, they happened with more frequency when the vagina and external genitals were involved.

Gummata of the Cervix.—The first definite information concerning syphilitic tertiary lesions of the internal organs of generation was published by Oppenheim in 1908. He admits, however, that very little was known of gummata of the cervix. While only isolated observations were recorded up to that time, he was of the opinion that gummata of the cervix is not as rare as many would believe. Oppenheim was of the opinion that there were two stages in the development of the lesion, first the gummatous nodule and later the gummatous ulcer; and this corresponds with our knowledge of the pathology of these lesions. The lesion first appears on the cervix as a nodule either single or multiple. Softening rapidly supervenes giving the cervix the soft boggy feeling, not unlike Goodell's sign in pregnancy, only more accentuated. This softening of the cervical nodule soon goes on to ulceration and it is in that form that the lesion is most frequently encountered. These ulcers are practically the same in appearance as gummatous ulcers occurring elsewhere. They are deep and sharp edged, sometimes kidney-shaped and covered by a grayish pellicle which can be easily wiped off. The edges are undermined and the ulcer has a punched-out appearance. There is no inflammatory reaction in the surrounding tissues. They are painless to the touch. When healed they leave a radiating scar which may cause a narrowing of the cervical canal. These lesions when healed not infrequently present an appearance not unlike leukoplakia lingualis.

Recently (in 1916) Gellhorn and Ehrenfels published a monograph in which they described 21 cases of cervical lesions caused by tertiary syphilis. In 1 of these the patient whose Wassermann was positive showed a tumor as large as an apple on the anterior lip. The uterus was much enlarged but freely movable and not tender. Excision of a piece of the mass showed histologic evidences of its being a gumma. Four weeks later the patient died. Upon autopsy the uterus was found to be involved completely in a gummatous process extending from the cervix to the fundus. Gummatous masses were also found in the right tube and ovary, the retroperitoneal glands, the liver and the lungs.

Breasts.—Chronic mastitis is a common occurrence in syphilitic women. Syphilitic tumors of the breast are not infrequently mistaken for carcinoma. Distinctly characteristic gummata can as a rule be diagnosed with comparative ease but in unilateral or bilateral chronic mastitis the differentiation from carcinoma is sometimes attended with great difficulty. Tertiary syphilitic lesions of the breast have been reported from the time of Anstruc. Lancereaux first distinguished between the diffuse infiltration of the secondary stage and the circumscribed gumma of the tertiary stage. Diffuse mastitis in the early stages of the disease has also

been mentioned by Von Zeissl. The subject is ably discussed by Burnier who gives examples of the condition from shortly after the appearance of the chancre to many years subsequent thereto. The possibility of syphilitic mastitis either as a diffuse gummatous infiltration or as single or multiple gumma should always be considered in the diagnosis of any growth or chronic inflammation of the female breast.

Menstruation.—Syphilis may be the causative factor in disturbances of the menstrual function. Menorrhagia and metrorrhagia may result from gummatous infiltration of the endometrium. The profound anemia which frequently arises in the secondary stage of syphilis in women may cause the function to disappear for a time. The menses may also be disturbed by inhibition of the harmonious synergism of the endocrine glands the result of syphilitic disease. Syphilis in women as in men is undoubtedly a cause of sterility.

In the secondary stage of syphilis in women who have just undergone a confinement or who have been subjected to an operation of the pelvic organs, a long continued, slightly remittent fever may be present. This is also the case in tertiary syphilis where there is a lesion of the generative organs that has been overlooked. This febrile movement if continued over an undue period of time and where no other cause can be assigned should always cause a suspicion of syphilis.

From the résumé contained in this chapter it must be admitted that syphilis occupies a more important position in the domain of gynecology than has been given it either by the general practitioner to whom these cases usually first present themselves or by the pelvic surgeon and specialist to whom they often later come for relief.

Latent Syphilis.—There is more latent or asymptomatic syphilis in women than in men and this form of syphilis is always potential of harm—the more so as it works unseen and under cover, as it were. In gynecology as in internal medicine remember the adage "When in doubt take a Wassermann." You may thus find what you did not suspect and, incidentally, add much to your credit as a diagnostician; at the same time your patient will be relieved whereas, without the Wassermann, she would not be.

CHAPTER XXVI.

SYPHILIS AND PREGNANCY.

THAT syphilis could be transmitted from the mother to the child yet to be born has been known since the days of Paracelsus. The influence of syphilis upon the pregnant woman and the product of conception has commanded the attention of syphilologists and obstetricians ever since. The knowledge gained in the past fifteen years has brought about many changes in the views formerly held, so that the aphorisms of the teachers of a former time have been relegated to the limbo of ideas no longer held as true.

Modern Views.—For many years Colles' law and Profeta's law (see Chapter XIV) went unchallenged. Coupled with the fact that florid syphilis in the pregnant woman was a frequent cause of abortion and still-birth, they represented practically about all we knew concerning the disease in its relation to child-bearing. But the discovery of the Treponema pallidum and the Wassermann reaction has changed all this and we now (since 1905) know the facts upon which these laws are based and our conclusions have been modified accordingly. Since 1905 the literature on the subject has been voluminous.

The Wassermann test has undoubtedly enabled us to arrive at a much clearer insight as to the incidence of syphilis than heretofore. We have learned that it is present, especially in a masked form, much more frequently than was supposed. We have also been made aware that absolute dependence cannot be placed on a serological reaction in diagnosing syphilis either in the pregnant woman or the child. This aberrancy of the Wassermann reaction I shall discuss in another place. We can also affirm, what was formerly denied, that paternal infection can and does occur, although but rarely.

Wassermann Reaction in Pregnancy.—The peculiarity which the pregnant woman exhibits toward the Wassermann reaction is shown in other ways that are still more puzzling. In pregnant or parturient women the milk may react positively and yet syphilis may not be present; the reaction, however, in these instances is never marked. Scarlet fever arising during pregnancy will cause a positive reaction, as will also carcinoma and puerperal sepsis. So too, patients with eclampsia almost always give a strongly positive reaction and yet

syphilis may not be present. In many of these patients, however, there is really a condition of latent maternal syphilis existing. These women may remain in good health indefinitely and yet convey syphilis to their offspring through the ovum, decidua or placenta.

Numerous observers have also found that too much reliance must not be placed in a Wassermann reaction made with blood taken from the umbilical cord. While it is perhaps wise to do this as a matter of routine, yet the absolute test is to search for the Treponema pallidum in the cord itself. The organism should be looked for in the walls of the vein and the connective tissue stroma. In a suspected case a section of the cord should be preserved in a formalin or Ringer's solution and later examined for the presence of treponemata. Examination of the placenta is not so reliable, as it not infrequently happens that the treptonemata cannot be found in the placental tissues, although the woman may be patently syphilitic. Usually, however, they can be found, and when present they indicate not so much the presence of active syphilis in the mother as its existence in an active form in the child. As strongly presumptive evidence of this is the fact that the organisms when found are always on the fetal side of the placenta. This is especially interesting because it goes far to prove that latent syphilis in the mother is undoubtedly derived from an infected fetus. The organisms may remain dormant, as it were, for an indefinite period and after the woman has borne several healthy children she may suddenly develop symptoms of the disease. It can thus be assumed with almost absolute certainty that infection of the mother occurs through the fetus by way of the umbilical vein or the ruptured vessels of the chorionic villi. In other words, her infection is a true syphilis d'emblée. The antigens thus formed allow the mother to nurse her syphilitic child with impunity, as stated by Colles long ago. But if for any reason she has not these antibodies she cannot nurse her child without grave danger of becoming infected herself, which goes to prove an exception to Colles' Law. On the other hand, if the mother is syphilitic and the child is proved to be free from the infection, she cannot nurse the child without infecting it.

From the facts just stated it can be inferred that Colles' and Profeta's laws no longer hold. The explanation of the paradox of the apparently healthy mother nursing her syphilitic child is to be found in the latent syphilis and the consequent antigens present in her blood and milk. The same is true of the apparently healthy child suckling from the syphilitic mother. It also is a latent syphilitic. Since we know that it is the fetus which conveys the disease, no woman can give birth to a syphilitic child without herself also being syphilitic; the disease may be, and often is, dormant for a long period of time.

The Placenta.—A clinical diagnosis of syphilis can be made from the placenta within certain limits. Evidences of the disease are to be found in the placenta in 70 per cent of all cases. This is true, in spite of the fact that the child may show no visible evidences of lues. It is apparent in some cases that the disease has exhausted itself on the placenta and in consequence the fetus is but slightly affected. This being so, infants who have inherited syphilis do not always show symptoms at birth and for a considerable time thereafter there are no symptoms in a large percentage of cases. The "little old man" appearance so graphically described by Diday is often missing and the infant at birth appears to be a perfectly healthy child. It has been said that syphilitic infants, even when not showing evidences of the disease at birth, are more hirsute than healthy infants. I have not been able personally to corroborate this. Again, the child may exhibit symptoms of syphilis and yet the placenta appear to be perfectly normal. This is the exception, however, rather than the rule; the placenta shows certain signs which, if not pathognomonic of the disease are, to say the least, strongly suggestive of it. Almost invariably there is a marked disproportion between the size of the placenta and the size of the child. In syphilis the placenta is decidedly larger. Between a normal placenta and a normal child the proportion by weight is approximately 1 to 6. In syphilis this proportion is changed to 1 to 4 or even 1 to 3. Pinard has pointed out that there is also a decided increase in the amount of amniotic fluid. In regard to this discrepancy in the proportion by weight between the healthy and the syphilitic child it must be borne in mind that it is possible for it to be more apparent than real because the syphilitic child is almost invariably under weight.

Syphilis of the maternal portion of the placenta may occur as a circumscribed or a diffused process. We are largely indebted to Fraenkel for our knowledge of syphilitic disease of the fetal side of the placenta. The pathologic changes in the placenta consist of swelling of the chorionic villi caused by a round-celled infiltration, and a considerable reduction in the number of bloodvessels. These changes, as I have already stated, vary in different portions of the placenta and according to the extent to which they are present the fetus will be undersized from lack of nutrition, or if these changes are sufficient they will cause the death of the fetus in utero. The umbilical cord shows similar changes; there is round-celled infiltration about the vessel walls, changes in the adventitia of the walls, the muscular coat and the intima, all of which are thickened and edematous from infiltrative processes and the lumen of the vessels, in consequence, is much reduced.

The syphilitic placenta is much increased in weight and size,

the stroma cells are increased to a marked degree and obliterative endarteritis and endophlebitis are present to a more or less marked degree according to the intensity of the infection. These changes may be said to be pathognomonic and afford very strong evidence of fetal syphilis, while their absence does not by any means exclude the disease. While the demonstration of the Treponema pallidum absolutely proves the presence of the disease, the absence of this organism by no means proves that syphilis is not present. I may say, in passing, that there are so many discrepancies between the histopathologic findings in the placenta and fetal tissues and the maternal Wassermann reaction, that many observers are of the opinion that this test is of less value for a correct diagnosis of fetal syphilis than the search for the Treponema pallidum in the placenta or cord. With these observations I am in full accord.

The syphilitic placenta shows deep sulci between the lobes, which causes the cotyledons to appear more prominent. Its color is much paler than the normal placenta, and its surface is covered with yellowish-white patches. Its substance is also extremely friable and on section has a mottled appearance that has been likened to sausage meat. The vessels of the cord are visibly thickened, although this sometimes occurs without syphilis. When the fetus is born dead the cord is often edematous and the vessels may be plainly seen, shining through the swollen cord. Wharton's jelly may be absent. The amniotic fluid may be increased to such an extent as to constitute hydramnios. This is to be accounted for by the placental lesions incident to the disease. It may, however, be due to a syphilitic hepatitis. The changes occurring in the placenta are in most instances the cause of fetal death.

Habitual Death of Fetus.—The condition known as habitual death of the fetus is frequently due to syphilis. The child dies in each succeeding pregnancy, usually between the thirtieth and thirty-fourth week and is soon thereafter expelled. It cannot be denied that syphilis tends to the formation of monsters and of children malformed to a lesser degree. It is not true, however, that recent syphilis transmits itself as congenital syphilis and tertiary syphilis as malformations. While syphilis is undoubtedly the most frequent cause of abortion—Charpentier found that in 781 luetic pregnancies there were 302 abortions, and Miller states that 70 per cent of luetic women abort—the consensus of opinion among modern observers is that syphilis does not cause abortion as frequently as was formerly supposed; nor does it follow that every macerated fetus is syphilitic.

Mangiagalli's Observations.—In the study of syphilis and pregnancy from the standpoint of the clinician, the observations of Mangiagalli are worthy of note. He recognizes four conditions: viz., both parents syphilitic when conception occurs; the mother

alone infected; the father alone infected; the mother becomes infected after conception, both parents having been healthy prior to conception. His conclusions are that an apparently healthy child born of a syphilitic mother is syphilitic although the syphilis is latent. When the mother becomes infected after the seventh month the disease in the child is apt to be less severe than if the infection occurred earlier in pregnancy. He could discover no direct relation between a positive Wassermann and the clinical manifestations of syphilis. When both parents are syphilitic the child inherits the disease in about 75 per cent of births. When the mother alone is syphilitic the child inherits the disease in about 60 per cent; while if the father alone is syphilitic the child inherits the disease in from 10 to 20 per cent.

The frequency with which abortion and premature labor occur as the result of syphilitic infection is universally recognized.

Premature Labor.—Syphilis may lead to delivery before term by reason of the intensity of the infection at the moment of impregnation, by which the embryo from the very beginning of its existence is so gravely affected that it dies and is expelled as a foreign body in the uterine cavity, by reason of syphilitic disease of the placenta and the fetal appendages. The placenta may be affected either on the fetal or maternal side. Premature labor or abortion may be induced by reason of the constitutional toxemia caused by the disease.

While it cannot be said with absolute certainty that every prematurely born child of syphilitic parentage, whether still-born or living, is syphilitic, we still possess abundant evidence that in the vast majority of instances such children come into the world infected with the disease.

Abortion.—The more recent the syphilis is in the woman the more apt is she to abort. But as the disease lessens in virulence with each succeeding pregnancy there is an increased tendency toward the birth of viable children. But it is undoubtedly true, however, that under the influence of proper treatment this tendency to still-births, abortions and premature labor may be cut short at once, and after one abortion or miscarriage due to active syphilis the woman may bear a healthy child.

When abortion occurs in the early months of pregnancy, *i. e.*, before the third month, the embryo is found to be more or less advanced in decomposition as the interval between its death and expulsion is long or short.

Miscarriage from syphilis usually occurs between the fourth and fifth months, and especially between the sixth and seventh months. When the amniotic fluid has been retained within the unruptured membranes it is turbid, dark and ill-smelling. The dead fetus expelled during the later months of pregnancy may show

evidences of syphilitic infection or, as not infrequently happens, there may be no visible signs whatsoever. The same may be said of still-born infants born at full term. In many instances, however, there are tangible evidences of the disease such as roseola, papules, blebs. In other words, the fetus has the same symptoms in the uterus that it would develop later if born alive. The infant born alive may show, for a time at least, absolutely no evidences of the disease, but certain alterations of the fetal appendages are usually present which are of considerable value in establishing a clinical diagnosis of inherited lues.

Observations of Fraenkel.—Fraenkel, basing his observations of fetal syphilis upon the presence of the epiphyseal osteochrondritis of Wegner, which is present in a very large majority of still-births and even of infants viable at birth, has reported his findings of the fetal side of the placenta as follows: The placenta is increased in weight and size. Its density is also considerably greater than that of the normal placenta. The fetal tufts are much infiltrated and there is an increased growth of the epithelium of the tufts. This round-celled proliferation leads to destruction of the tufts and obliteration of the vessels supplying the tufts. As expressive of the process, Fraenkel has given the term "deforming granulation infiltration of the fetal villi." The fatty degeneration that quite frequently accompanies this infiltrative process is a complication and is not necessarily pathognomonic. Fraenkel regards the thickening of the epithelium covering the villi as a result of the hardening of the villi in the pathologic amniotic fluid. Fraenkel is of the further opinion that the changes when occurring by themselves are to be attributed to a paternal transmission, and when the mother was infected before or at the time of conception endometritis placentaris gummosa is prone to occur along with the disease of the fetal villi.

While the facts I have just related are very patent in many instances, it is quite possible for the placenta of a syphilitic child to remain healthy. Especially is this true where the mother has become infected during the latter part of pregnancy when it sometimes occurs that both fetus and placenta remain free from the disease.

The position of Fraenkel is about as follows: Where syphilis is transmitted by the father directly to the ovum, the conditions just described will occur. Where the mother becomes syphilitic by conception, this diffuse syphilis of the villi may occur along with endometritis placentaris; where the mother before conception was syphilitic, or became so shortly after, it is possible for the placenta to remain normal or it may develop syphilis on both the maternal and fetal sides. Finally, if the mother becomes infected after the

seventh month of pregnancy, the chances are that neither the placenta nor the fetus will be affected.

Sterility.—It has been observed that syphilitic women are often sterile because of disturbance of the function of the ovaries, the same as many syphilitic men are sterile because of testicular disturbance caused by the disease.

Effects of Syphilis.—The actual effects of lues vary with the length of time of infection and upon the treatment the patient has received. It is undoubtedly true that well treated patients almost always give birth to healthy children. When the syphilis is recent and untreated or inadequately treated, the product of conception dies and is expelled. Subsequent pregnancies terminate in the same way but after a longer period of gestation, until finally a living but syphilitic fetus is born, and later a living and apparently healthy child may go to term. This child may develop syphilis within a few months of birth, or the appearance of the disease may be delayed until puberty or adolescence, or it may never show any signs of the disease.

It has been stated that 83 per cent of repeated abortions are due to syphilis; but at present there are some who deny that syphilis causes abortion as frequently as has been supposed. With this latter view I most emphatically disagree. I am convinced that syphilis is the most potent of all causes of abortion, miscarriage, premature birth, and of dead fetus at term. The facts as they are known to us can allow of no other conclusion.

Labor.—During labor, in a woman with active syphilis, the pains may be weak and the progress of the labor consequently slowed. In dead-born children abnormal presentations are the rule. Cicatrices from a healed ulcer of the cervix may greatly impede labor, and may necessitate incision of the cervix, craniotomy, or even Caesarian section.

Syphilis in Pregnant Woman.—In a pregnant woman syphilis assumes a more severe form than in the non-pregnant. The chancre is larger and persists for a longer time. Mucous patches or condylomata are larger and more rebellious to treatment. The reason for this is the increased vascularity of the parts. Secondary symptoms, especially on the genitals, appear earlier than in the non-pregnant. Eroded papules are apt to appear on the vulva, as has been observed by Fournier, "they develop with a singular exuberance, take on quickly a granulating condition, hypertrophy, and often constitute veritable tumors, which invade and deform the entire vulva."

In pregnancy the anemia is always more profound than it otherwise would be, the headache, insomnia, and bone pains are also worse.

According to some observers, direct paternal infection of the ovum by the semen is impossible. Again it is asserted by some that paternal infection of the ovum is possible but that it is always associated with infection of the mother, that this is not infrequent and that the mother may thus become infected through the embryo. The probabilities are, however, that in the majority of instances the embryo is infected by the already infected mother, either by infection of the ovum whilst in the Graafian follicle as part of the mother's constitutional disease or by transplacental infection. In certain instances, both father and mother infect the child.

It is possible, but not in my opinion probable, that some very early abortions may be the result of paternal infection of the ovum, and the woman may escape infection owing to the expulsion of the ovum before fetal circulation is established. According to some, the semen may be the only fluid in the body that is infectious. Levaditi and others have found the Treponema pallidum in the ovum.

While Finger and Landsteiner succeeded in inoculating apes with syphilis with semen from a syphilitic in the secondary stage of the disease, thus proving beyond doubt that the semen was infective and therefore contained the Treponema pallidum, it was not until 1920 that Pinard was able to demonstrate the organism in the seminal fluid. The size of the Treponema pallidum would seem to preclude its being found in the spermatozoön but when we realize that it is possible for the organism to roll itself up, as it were, it does not require any great stretch of the imagination to believe that it can be contained in the spermatozoön. Recently Milian claims to have seen the organism molded in the head of a sperm cell. In 1736 Anstruc wrote, "The semen and the other seminal fluids are mostly submitted to infections by the venereal virus, on account of the particular affinity which make them apt to enter it most intimately." More than one hundred years later —in 1864—Diday expressed a similar opinion when he wrote, "The sperm can directly infect, and the spermatozoön, which is the transmitter of the essential element has power enough to infect the ovule and the organism of the woman." Even if it had not been demonstrated that the Treponema pallidum could be found in the spermatozoön, the analogous discovery by Koch of the Spirochæta duttonii and by Levaditi and Manouelian of the spirillum of Brazilian pyemia in a similar situation would prove that it is possible for the Treponema pallidum to be transmitted by the spermatozoa direct.

Carle is of the opinion that women infected in this manner react differently to the disease from those infected in the usual way who show a chancre. I believe this is possible and probable.

According to Vidakowich the semen of syphilitic men contains

56 abnormal spermatozoa to every 1000, whereas in healthy men this ratio is only 10 to every 1000 spermatozoa. It is probably by means of these pathologic spermatozoa impregnating the ova that paternal transmission of syphilis occurs. Therefore it can be stated as an axiom that cannot be denied, that every syphilitic man—even if the only evidence of the disease is a positive Wassermann reaction in his blood—is potentially the father of a syphilitic child.

It must be remembered that parturient women with tuberculosis, malignant growths, or eclampsia, may give a positive Wassermann.

Syphilis a Grave Complication.—Syphilis, it may be truly said, is always to be regarded as a grave complication of pregnancy. It increases puerperal morbidity more than any other cause. Many cases of nephritis with its concomitant eclampsia can be traced to syphilis. Sepsis is more apt to occur in syphilitic women than in those who are free of the disease. Cicatricial stenoses of the os due to syphilitic lesions may cause undue delay and complication of labor. The same is true of edema of the cervix due to active syphilis.

Thus it will be seen that syphilis is perhaps the most important of all the complications of pregnancy. Not only does it threaten the mother, but her unborn child as well. For it is well known that a comparatively small percentage of syphilitic infants reach maturity. Also, it is well known that those who do reach maturity are handicapped most cruelly in the struggle of life. If syphilis is suspected in a pregnant woman, she should be vigorously treated, and there is no exception to this command. The finer details in the treatment of women, wherein they differ from the treatment of the disease in men, are discussed in the chapter on Treatment.

CHAPTER XXVII.

SYPHILIS AND PEDIATRICS

Syphilis is of perennial interest to the pediatrician because he encounters it at every turn either in its frankly congenital form, or as the cause of a dystrophy, or in some of its many disguises whereby his skill is taxed. As in adult life syphilis is a factor of great moment in the life of the child and our vigilance should never be relaxed in searching for it.

Frequency of Syphilis in Children.—The clinical recognition of congenital syphilis is not always easy despite the assertions so glibly set forth in many text-books. This is exemplified by the statistics given by some authors before the advent of the Wassermann reaction. For, if we base our findings of congenital syphilis strictly upon the results obtained by the Wassermann test it will be found that the disease is much more frequently present than is usually supposed. According to the statistics collected by Churchill and Austin the proportion runs from 2 to 16 per cent. These figures represent only those observed in the United States; and there is every reason to believe in some of the more backward foreign countries the incidence of the disease as an inherited dyscrasia is much higher. Further, these figures by no means represent the incidence of the disease even in such a favored land as ours, since they do not include the numerous infants who die within a few hours or days after birth; nor do they include the prematurely born infants who gasp out their lives within a few minutes of their entrance into the world; nor do they include the number of those born dead, or the abortions and miscarriages due to the disease.

The pediatrist is chiefly concerned with the congenital form of the disease but as I have already stated this also includes many occult dystrophies and dyscrasias which on their face are not recognized as such. To still further complicate matters in many of these cases the Wassermann reaction is not positive, especially in later childhood or early adolescence when the activity of the disease is lost but not the impress therefrom.

Kassowitz Law.—It may be stated as a general rule that the less recent the disease is in the parents the better the state of nutrition of the child will be, despite the fact that it has syphilis. This is more or less in accord with the so-called Kassowitz law which I have

mentioned in the chapter on Syphilis and Pregnancy. That is, attenuated syphilis in the parents will usually be transmitted as such in the offspring, although this does not always hold good. It is probably because of this attenuation that the later children of syphilitic parentage sometimes escape, or if they are born with the taint it is these children which survive rather than those which were born when the disease was active.

Prognosis Poor.—While countless thousands of infants and children die from congenital syphilis it is not from the *lesions* of the disease they succumb, unless they involve such viscera as the heart, lungs, liver or brain; rather is it due to the profound *toxemia* and the consequent depression of the vitality both of which render the infant an easy prey to some intercurrent affection such as pneumonia or intestinal disorder. The congenitally syphilitic child is poisoned at the very beginning of its life and its vital urge cannot overcome even the slightest handicap. As Fournier said long ago, these children have an "inaptitude for life." For that reason the degree of marasmus present in a syphilitic infant is an important factor from a prognostic standpoint. It must also be borne in mind that even when these infants and children are treated skillfully and are otherwise accorded the best of care, the disease will show a tendency to relapse which can hardly be overcome. I do not mean to infer that this occurs in all cases, but in an appreciable percentage. The chances of ultimate recovery are illustrated by the statistics of Hochsinger. He analyzed a series of 263 cases under observation from four to twelve years; of these 79 died, 112 were in more or less poor health, and 72 were entirely well.

The duration of congenital syphilis is uncertain. In the large majority of cases the disease has spent itself by the eighteenth year; and thereafter except for dystrophies caused thereby the person so affected may go through life without any further manifestations. This does not always hold however; many an ailing man and woman goes through a life of chronic invalidism because of the taint inherited from the parents.

Under proper treatment in well nourished infants the skin lesions usually disappear in a few weeks or a month at most. The glandular enlargement and the inflammation of the nasal mucosa—"snuffles"—usually persist for a longer time. The disappearance of these superficial lesions does not imply however, that the disease is cured. The late appearance of tertiary symptoms is evidence of this.

Nervous System Involved.—As in the acquired disease, the nervous system frequently bears the brunt of the attack in congenital syphilis. Even if no definite lesions exist the central nervous system of these children is almost invariably unstable. Convulsions, paroxysmal vomiting, enteralgia and nocturnal enuresis are

frequently observed. Later there may be attacks of migraine or epileptoid seizures.

Mental Deficiency.—Feeblemindedness, imbecility and idiocy are frequently caused by syphilis. In 78 cases of feeblemindedness, imbecility and idiocy examined by Gordon, the Wassermann reaction was positive in 50 per cent. White estimates that 20 per cent of mental defective are so because of congenital syphilis.

Syphilis versus Scrofula.—Congenital syphilis is frequently diagnosed as "scrofula" even in these days of the Wassermann test. In my opinion the majority of these so-called scrofulous children are syphilitic and the lesions manifest are as often syphilitic as they are tuberculous. No involvement of the bones, joints, glands or skin should escape the Wassermann test.

That syphilis plays an important part in many of the diseases of childhood of a chronic character is coming to be believed more and more. Especially is this true in regard to those obscure syndromes which have their origin in some dysfunction of the endocrine system. It is these bizarre cases, occurring in children from five to fifteen years of age, that syphilis should be especially sought for. It happens more often than not that syphilis is the underlying basis of some organic perversion or dystrophy that is the cause of the symptoms.

Syphilis versus Perlèche.—A disease often seen in childhood and which may be mistaken for syphilis is perlèche. It is probably a streptococcal infection and belongs to the impetigo group of dermatoses. Most frequently it is observed at the commissures of the lips as patches of white, moistened epithelium which constantly exfoliates giving rise to fissures not unlike the rhagades of congenital syphilis. They sometimes bleed quite freely. Their characteristic appearance and rebelliousness to treatment may arouse a suspicion of syphilis which may only be allayed by a Wassermann test.

Tinea, lupus, impetigo, eczema and pemphigus may at times be mistaken as manifestations of syphilis. The Wassermann reaction and careful attention to diagnostic detail, will, however, determine them.

Acquired Syphilis.—In infants and children under puberty acquired syphilis is rare, yet undoubtedly it does occur and as such must of necessity be *syphilis insontium*. It has been stated that acquired syphilis in children is usually of a very mild type. It has also been stated that syphilis acquired in infancy or childhood is apt to be malignant and difficult to control. In my opinion constitutional resistance is the main factor in determining the severity or mildness of a given infection. The sources of infection, as would be supposed when the disease was acquired innocently,

are extremely varied. The various modes whereby the disease can be transmitted I have discussed elsewhere and shall therefore not repeat them here. The face, scalp and lips are the most frequent sites of extra-genital chancres appearing in children and suspicious sores appearing on these parts should be carefully investigated as to the possibility of their being syphilitic. Extra-genital chancres occurring in infancy or childhood, like extra-genital chancres occurring in adults are usually atypical. It cannot be denied that this helps to confuse the diagnosis. One feature of these infantile extra-genital chancres, however, which is worthy of note is that the adenopathy which always accompanies the chancre is less noticeable than when it occurs in adults. Unfortunately the physician when called to examine a child because of a sore or eruption on the body, rarely if ever, thinks of acquired syphilis. Or, if he thinks of syphilis it is of the congenital form of the disease. For that reason acquired syphilis in infants and children often goes unrecognized for a considerable period and thus makes headway which later may be difficult to overcome. The diagnosis of acquired syphilis in these cases is admittedly difficult. The almost invariable aberrant location of the chancre, which because of this it is so often overlooked, the comparative rarity, and the difficulty in many instances if the disease is at all advanced, of distinguishing between congenital syphilis are the factors that make it so. Again, there is the possibility of a fresh infection being grafted on an infant or young child that is already congenitally syphilitic. This is, of course, a most rare occurrence, but such a complication has been recorded by no less an authority than Gaucher.

Acquired Syphilis versus Congenital Syphilis.—The roseola which appears in the acquired disease cannot be distinguished from that which occurs when the disease is congenital. The same is true if the eruption is papular or pemphigoid—these two as in the congenital form presaging a severe infection. If the secondary eruption is roseolar it is usually more pronounced than when occurring congenitally, but, as such, offers no other criterion in differentiation. Therefore, a rash developing suddenly on an otherwise healthy infant or young child (after the usual exanthemata of early life have been eliminated) especially if the rash is accompanied with fever which persists for several weeks and is accompanied with marked prostration, should arouse a suspicion of acquired syphilis.

Sequelæ.—The constitutional sequelæ following an initial lesion acquired in childhood differ but little from those occurring in adults. The difference is to be noted, as I have already observed, in the eruption being more pronounced and in the greater degree of prostration as measured by fever, malaise, rheumatoid pains and other symptoms of the toxemia. Gaston states that "Syphilis contracted

in the first days of life gives rise to similar malformations, dystrophies and arrests of development to those supervening on intra-uterine infection." With the distinguished French author I take issue. While it is possible, even probable, that neglected acquired syphilis in infancy might produce dystrophies and arrests of development, yet these would not, in my opinion, compare with those of congenital syphilis in severity or multiplicity because of the fact that in congenital syphilis the infection dates from the origin of the child *in utero*. From knowledge based on pathologic facts we know that the acquired infection cannot possibly be as intense as when it occurs congenitally. For that reason, if no other, acquired syphilis in an infant cannot be as severe, all other things being equal, as when it exists in the congenital form. It must not be forgotten however, that acquired syphilis in childhood or infancy may be as malignant and fulgurant as sometimes occurs in adult life.

Prognosis.—The prognosis of acquired syphilis in infancy is on the whole, very much better than in the congenital form.

Differential Diagnosis.—The differential diagnosis of the congenital from the acquired disease is often a matter of much difficulty but in the main the difference is to be found in the absence of visceral involvement in the acquired form and its early presence in the congenital. It is also possible to obtain a history of a chancre or of a persistent sore from which the infection could be dated. Epiphysitis or pseudoparalysis of Wegner is frequently noted in congenital syphilis while it is never present in the acquired disease. The characteristic coryza or "snuffles" is also absent in acquired syphilis while it is almost invariably present if the disease is congenital.

Treatment.—The treatment of acquired syphilis in infants and children is identical with that for congenital; that is it resolves itself into the administration of arsphenamine and mercury. There is one difference however, which is most important. In congenital syphilis arsphenamine should always be preceded by mercury. In acquired syphilis arsphenamine should precede mercury. Arsphenamine should be administered according to the weight rather than to the age of the child. The dose should be 0.01 gm. to 12 kilos, *i. e.*, two ounces of arsphenamine solution to twenty-five pounds of body weight. If an infant weighs twelve pounds it should receive 1 ounce of the solution. The drug should be given intravenously. This is not difficult if injected into the jugular vein, or in one of the veins on the vertex of the skull. I prefer the jugular. A fine needle should be used, and if inserted into the jugular vein, the child should be firmly held with its head hanging over the edge of a table. It will invariably cry and this will cause an engorgement of the vein, which will then become prominent and can be easily

penetrated. The injections should be given at intervals of four or five days, and the number of injections should be regulated by the disappearance of the symptoms and by the phases of the Wassermann reaction.

Mercurial Treatment.—Mercury can be given either by mouth in the form of gray powder or by inunction either with the weaker mercurial ointment (33.3 per cent) or with the oleate. After each inunction the skin should be powdered with starch or talcum powder and later washed with soap and water. A different part of the body is to be used for each inunction.

A nursling that acquires syphilis should be taken from the mother's breast if she is free of the disease. The diet should then be made to conform to the age and strength of the infant. Personally I prefer a modified milk formula in which the fats, carbohydrates and proteids most nearly agree with those composing the mother's milk at the time the child is weaned. This question of feeding is most exhaustively treated by Holt in his text-book and to it I refer the reader.

CHAPTER XXVIII.

SYPHILIS AND GERIATRICS.

"Syphilis does not love the old;" said Ricord, "it plays them a hundred tricks which it does not try on the young." Fournier expressed the same opinion when he said: "Syphilis kills old persons and children in a way not to be found in regard to adults."

Syphilis Uncommon in the Aged.—Syphilis acquired in old age is comparatively rare. According to Sigmund, extragenital chancres are more frequent in the aged than in those younger in years. This may be so, but I am quite certain however, that extragenital chancres are not as frequent in the aged as they are in children. When syphilis is acquired after sixty years of age it usually presents certain differences in its evolution and its impress on the organism than when the disease is acquired in youth or middle age. Syphilis when contracted in old age is on the whole more severe. This is the opinion of nearly all syphilologists. The only exceptions being Sigmund and Lagneau. Sigmund during thirty years collected 118 cases, of which 87 were in men and 30 were in women. From an analysis of these cases he came to the conclusion that the disease was milder and more amenable to treatment if acquired in old age than when acquired in those of younger years. Lagneau asserted that "The rigidity of the vessel walls and the diminished vitality of the tissues are an impediment to the quick development of the symptoms." I am not in accord with these conclusions. From a study of 40 cases Dulac observed that senility aggravated the disease and that its manifestations were more pronounced and yielded less readily to treatment. The same facts have been observed by Regoby, by Gailleton and by Lebard. The frequency and early appearance of nervous lesions in syphilis acquired late in life has been noted by many observers including Engelsted, Braus, Gjor, Fournier and Wile.

Syphilis in the Aged is Serious.—It is not difficult to understand why syphilis in senescence is a grave infection. If we consider the body as a machine (which in a sense it is), it must be remembered that in old age it must be more or less worn out. If there were any flaws in its make up they will surely be showing now; any diseases or the sequelæ thereof will now be exerting their maximum influence. At this period of life the cell elements of which the body is composed will be undergoing retrograde metamorphosis. The tendency of

all the tissues is toward shrinkage—fibrosis. The vital activity is declining; the reserve that once could be brought into action to overcome the noxious influences of disease no longer exists. When the syphilitic toxemia permeates a body already decrepit with age and in all probability rendered still more so by wide spread arteriosclerosis, crippled kidneys, valvular or myocardial disease, rheumatic or gouty diathesis, impaired digestion and chronic constipation, pyorrhea and decayed teeth, it is to be inferred that its effect will be severe.

Chancre in the Aged.—The period of incubation of the chancre in youth or middle age is from three weeks to a month. It may be longer; it may be shorter; but such is the exception. In old age the period of incubation is long—five to seven weeks. In the young or middle aged, unless cachetic from diabetes, alcoholism, or tuberculosis, the chancre is usually a benign and even an insignificant lesion. Many times the patient is not aware of its existence and in after years denies in good faith ever having had such a sore. In the aged the chancre is a pronounced and distinctive lesion. It is large and frequently of the type spoken of as a "beef-steak" chancre. Often it is phagedenic, and if situated extragenitally its indolence in healing frequently gives rise to the suspicion of malignancy. This slowness in healing is characteristic of the primary lesion in the aged. So also is the degree of induration, which is much in excess of that encountered in younger persons. When the chancre has healed the induration persists for a much longer time than is usual in younger patients. The lymph glands in the vicinity of the sore are also harder than they are in younger persons. As the infection becomes more generalized this hardness—they often feel like stones beneath the skin—is to be noted in all the glands that can be palpated, the epitrochlear, the cubital, the axillary.

The so-called second period of incubation, that is the time between the appearance of the chancre and the appearance of the secondary eruption, is short. The eruption is nearly always papular. The roseola which is so frequently seen in younger syphilitics is conspicuous only by its absence. Papular syphilides of the palms of the hands and of the soles of the feet are frequently concomitant with the generalized eruption. Mucous patches on the lingual and buccal surfaces and on the pharynx—syphilitic angina, appear with startling promptness. Strange to say however, these lesions so typical of early syphilis in younger persons are only rarely encountered about the anus and genitals. Besides the mouth and tongue they are very frequent between the toes. Iritis frequently develops—so frequently, that its presence in an aged person should cause recently acquired syphilis to be suspected. It was observed by Lebard in one-third of his cases.

General Health in Aged Syphilitics.—Synchronously with the secondary stage of the disease as manifest by the papular eruption, the general health, which previously may have been excellent, undergoes a rapid decline. So often does this swift deterioration of the bodily forces happen that it may be regarded almost as pathognomonic. There is loss of weight and strength, headache and pains in the bones and joints, fever, anorexia—all the symptoms in fact of a more or less profound toxemia. Unless this asthenic condition is promptly met with antisyphilitic and supportive treatment it may cause the patient's death in a comparatively short time.

Severity of Tertiary Lesion.—In the aged the secondary period is materially shortened and the tertiary manifestations are precocious and severe. Cutaneous and osseous lesions are frequent, and unless treated with promptness and vigor may be very destructive. Before the Wassermann reaction came into use such lesions were not infrequently mistaken for malignant disease. Equal in frequency and much more disastrous in results is the involvement of the central nervous system, such as acute meningitis of the base or the convexity, gummatous infiltrations of the nerves of special sense, hemiplegia, monoplegia and spastic paralyses. All of these conditions frequently occur—much more so than they do in those of younger years.

Treatment.—The treatment of syphilis when acquired in old age should not be intensive. The principal objective should be to conquer the symptoms and not, as in younger patients to render the body sterile to the infection as evidenced by a permanent negative Wassermann reaction. To completely sterilize the tissues which is the object to be attained in younger persons is rarely possible in the aged. The state of the kidneys in old persons is often such that an attempt to do so would in many instances be extremely hazardous. If the disease can be held in abeyance as it were and the active lesions promptly made to disappear, this is all that can be expected or attempted.

Before commencing treatment a strict inquiry should be made into the state of the kidneys, the liver and the cardiovascular system. If these are seriously affected the treatment should be tentative from the beginning. By that I mean that the dose of the drug used should be well below the average dose and the intervals in which it is given should be wider apart than otherwise. Neoarsphenamine or silver arsphenamine should be given; of the first not more than 0.3 gm. in 30 cc of distilled water; if silver arsphenamine is used the dose should not exceed 0.2 gm. The interval between each dose should never be less than three days. Since the advent of organic arsenic I have discontinued mercury in these cases because mercury is much more nephrotoxic than organic arsenic

and it is the kidneys in these elderly patients that we have most to fear. As to the number of injections, it is impossible to say how many should be given; the symptoms must be controlled, and the prostration should be replaced by a sense of well being; this can be accomplished by the freeing of the lecithin bodies by the organic arsenic. In addition to the antisyphilitic treatment, the patient should also have supportive treatment, that is abundant and concentrated food such as the yolks of raw eggs, cream, milk sugar, small quantities of whisky, fresh air and quietness of mind. Iodide may be given to hasten resolution of gummatous infiltrates and it is especially valuable after arsphenamine treatment of nervous lesions. The sodium salt should be given in preference to the potassium as being less depressive.

Care in Treatment.—Bold or reckless treatment is not permissible in treating old persons who have recently acquired syphilis. By that I do not mean to infer that the treatment should not be vigorous but vigor should at all times be tempered with caution. Treat the symptoms, not the disease; and always remember that you are dealing with a worn-out body which cannot stand much stress in the way of toxic drugs.

CHAPTER XXIX.

THE SYPHILITIC FACTOR IN OTHER DISEASES.

It was the French syphilologist, Diday, I believe, who said, "Syphilis is a dung heap upon which all kinds of rottenness can grow." Present knowledge has since confirmed his words. The relation which syphilis bears to other diseases as a predisposing and modifying factor is most intimate and widespread. The influence which it exerts is always unfavorable, and as a creator of diseases which on their face do not carry the stigma of their cause it stands unequaled and alone. Long ago it was said that syphilis in itself constitutes an epitome of pathology. As Hutchinson has said, "There is scarcely a malady which has received a name which may not be simulated by it, and still fewer which it may not modify." Our increased knowledge as to the syphilitic element in so many diseases is due to the discovery of the cause of the disease—the Treponema pallidum and to the serum reaction in the blood of syphilitics made known by Wassermann. What was in former times a matter more of inference, now rests, because of these two epoch-making discoveries, upon the solid basis of a demonstrated fact. While there are undoubtedly exceptions to this statement, as there are to all others of a similar dogmatic nature, the co-existence or preëxistence of syphilis does not always imply that a condition is syphilitic; but in all obscure and chronic diseases whatsoever, I cannot emphasize too strongly that it is wise—it is very wise—to consider syphilis as the disturbing element. As an eminent internist once remarked, "When in doubt take a Wassermann." To this I might add, even when not in doubt take a Wassermann, because you may thereby learn something that you did not know before.

The influence of syphilis as a causative or modifying factor in other diseases is often occult, and extremely difficult to prove. Nevertheless if it exists it must be reckoned with. It is needful, therefore, to study and know well the case before resorting to the measures of the laboratory, which, after all, depending as they ultimately do upon the personal equation of the individual performing the test, are also liable to error. Careful clinical investigation will, at least, materially help and strengthen the opinion of the laboratory technician. For the diagnosis of disease by observation

and contact is one of the highest attainments in medicine, and he who depends entirely upon laboratory findings only confesses his lack of skill.

Prevalence of Syphilis.—In so far as the incidence of syphilis is concerned, "Syphilis is the despair of statisticians" as Osler says. Strange as it may seem it is not even mentioned in some figures as a cause of infant mortality, and among infectious diseases it ranks below cerebrospinal meningitis; and yet tabes and paresis cause more than half as many deaths as occur annually from typhoid. Of all the still-births occurring each year a most conservative estimate would be that one-half are caused by syphilis. In the first year of life several hundred thousand children die annually. It is a most conservative estimate that fully one-fourth die of syphilis. Those that are syphilitic and survive are frequently subjected to innumerable maladies. It is an old saying that "syphilis never kills," but the United States census reports more than ten thousand deaths due to syphilis, including tabes and paresis every year. When we consider that syphilis also causes meningitis and new growths in the brain, apoplexy occurring before fifty years of age, a predisposition to tuberculosis, arteritis, aneurysm, angina pectoris and other cardiovascular diseases, it can be readily appreciated that as an actual cause of death the incidence is far higher than is given. Actuarial reports both in the United States and Europe agree that uncured or rather latent syphilis, which is practically the same thing, very materially shortens life, and those applicants who are known to have had the disease are rated higher than those who are free from it. The Actuarial Society of America has shown that the mortality of syphilitics, even amongst selected risks, that is risks living among the best surroundings, is in excess of that of post-tuberculous hip-joint disease and of non-abstaining liquor dealers. The last class is rated the highest of all by statisticians throughout the world. Yet their death-rate is not as high as that of syphilitics. As Bloxam, of England, sums it up: "After twenty-five years' personal experience in the treatment of syphilis, I cannot think that any man who has had syphilis can be rated as a first-class life. The mere fact of his having had syphilis at once places him in a second-class division. No case with any secondary symptoms is insurable, nor is any case with distinct tertiary lesions. Syphilis lowers the vitality of individuals, and any person who has had it is liable to tuberculosis, chronic irritations, cancer and so forth. Therefore it is not possible to accept any man who has had syphilis as a first-class life; he should be taken with an addition to the premium."

I am not willing to go quite as far as Bloxam has gone in his assertions. I believe that syphilis is curable. By that I mean

that the Treponema pallidum can be completely eradicated from the system if proper treatment is instituted at the proper time. Bloxam's statement therefore would apply only to those cases which upon examination show a positive Wassermann or where the cytological findings are indicative of syphilis. Modern methods of treatment intelligently carried out have rendered almost obsolete the ancient saw, "once syphilitic always syphilitic."

The affinity of the treponema for the nervous system and the bloodvessels accounts for the high morbidity and mortality of syphilis. Approximately ninety thousand deaths occur each year from cardiac disease. Our widened knowledge compels us to believe that a large percentage of those deaths are due to syphilis. The result of Warthin's researches in cardiac pathology confirms this view. Many physicians are slow to ascribe cardiac diseases to syphilis yet the fact has been known since the days of Anstruc and Morgagni.

It cannot be gainsaid that the Treponema pallidum is the most notable of all pathologic microörganisms, for it is present everywhere.

In a general way it may be stated that syphilis is to be considered as a causative or influencing agent in all diseases of the nervous system, all circulatory diseases (especially aneurysm), all bone and joint diseases, all diseases of the eye involving the optic nerve, retina, choroid, sclera, iris or lens, all diseases of the liver and digestive diseases of prolonged chronicity, growths of all kinds and all lymphatic enlargements and all constitutional and metabolic diseases.

Barker of Baltimore has given a list of nineteen conditions which should cause an examination for possible underlying syphilis. These are, in the order given by him, as follows: "(1) Long-continued fever otherwise unexplained; (2) obscure nervous cases, both functional and organic; (3) chronic laryngitis, tracheal and bronchial stenosis, bronchiectasis and unexplained infiltrations of, or masses in the lungs or pleuræ; (4) aneurysms; (5) aortic insufficiency, especially when unaccompanied by other valvular lesions; (6) heart block and other cardiac arrhythmias; (7) arterial and venous thrombosis; (8) certain grave anemias; (9) paroxysmal hemoglobinurias; (10) indolent nodules in the tongue and tonsils; (11) enlargements of the liver and spleen; (12) strictures of the rectum; (13) atypical joint disease, and especially obscure diseases of the spine; (14) thickening of, or nodules in, the bones, especially when accompanied with nocturnal pain; (15) unusual forms of renal disease; (16) chronic orchitis, or nodules in the testes; (17) repeated miscarriages without apparent cause; (18) still-born children; (19) in disorders of metabolism and of internal secretion, especially in bizarre cases."

He also states further: "Among the many conditions often believed to be luetic in origin, in which sometimes it had to be admitted that a luetic factor was present, but which often occurred in the entire absence of lues, were the following: (1) Cerebral apoplexy; (2) high blood-pressure cases; (3) contracted kidneys; (4) multiple sclerosis; (5) certain suspicious lesions, especially those due to sporotrichosis or blastomycosis of the bones, lungs or subcutaneous tissue; (6) psychoneurotic states accompanied by syphilophobia; (7) Graves' disease."

It will be seen that the diseases listed by Barker cover a wide field yet it by no means exhausts the number of those diseases the presence of which is strongly suspicious of a syphilitic taint. Of these I shall mention Raynaud's disease which is now admitted to be of syphilitic origin in most instances. Leukemia can be, and not infrequently is, caused by syphilis. Long ago the Frenchman, Parrot, tried to show that rachitis was always due to syphilis. His views were held to be erroneous, but now we know that Parrot was at least half right because nearly one-half of these cases give a positive Wassermann. Dwarfism and giantism are both known to be expressions of heredosyphilis. Pott's disease while generally regarded as a tuberculous affection may also have a syphilitic etiology. Clinically the two conditions cannot be differentiated. Articular syphilis may simulate rheumatism or arthritis deformans so closely that it is impossible to differentiate between them. Syphilis is a frequent cause of acute yellow atrophy of the liver. The dictum of Hudels: "In every obscure affection of the liver suspect syphilis" is absolutely true. Syphilitic thyroiditis can cause the syndrome known as Basedow's disease; syphilis of the adrenals, Addison's disease; syphilis of the hypophysis, acromegaly.

Syphilis exerts a very unfavorable influence upon malaria. Syphilis grafted upon tuberculosis of the lungs hastens the progress of the latter; and if the syphilis occurs first, it undoubtedly predisposes in the susceptible the development of the tuberculous infection. Syphilis can simulate any known skin disease and it is admitted by all dermatologists that it reacts most unfavorably on any chronic dermatosis that may be present when infection occurs. In this connection I would mention vitiligo. Until recently its cause was unknown but it is now regarded as a positive stigma of syphilis, especially hereditary syphilis. In about 10 per cent of baldness there is a positive Wassermann reaction. Herpes zoster is sometimes present in syphilis, probably secondary to a localized meningitis. Scleroderma is sometimes present both in acquired and hereditary syphilis.

Syphilitic Nervous Diseases.—The proneness of syphilis to attack the nervous system is well known, but there are facts pertaining

thereto that are not so well known. I shall endeavor briefly to bring them to the attention of the reader. Many nervous diseases have symptoms that are pathognomonic of their syphilitic origin, but there are others which, while originating from syphilis, have neither subjective nor objective symptoms connecting them with the disease. It can be truly said that nervous syphilis parallels in its clinical display every organic and many of the functional diseases of the nervous system. Especially is this true of chronic nervous diseases. Syphilis should be suspected in every disease of the nervous system where the cause is not obvious, in every case where the symptoms vary from the usual and where there is a multiplicity of symptoms. Nervous lesions due to syphilis are much more amenable to treatment than those arising from other causes. This fact must be considered in diagnosis. It is also well to remember that pathognomonic symptoms rarely occur early, but appear only after the disease has become established.

Trauma and Syphilis.—Trauma can show that syphilis is present both by local and general manifestations. The trauma may increase the severity of certain symptoms or it may hasten the rapidity of their evolution. Syphilis can also react on the traumatism by aggravating it or causing local manifestations that retard resolution.

Nephritis and Syphilis.—A disease which is most common as every practitioner of medicine well knows is chronic interstitial nephritis or Bright's disease. It has long been the fashion to ascribe its cause to alcoholism. This has even extended to the laity. While alcohol may be a factor, it is not so well known that syphilis is also, and in my opinion and that of others who have studied the problem, a far more important one than that of alcohol.

Still has clearly shown, in his masterly monograph, that interstitial as well as parenchymatous nephritis is a very frequent concomitant of hereditary syphilis. He is inclined to believe that the interstitial type in some cases is even antenatal. With him I agree in every detail. It is known to all syphilologists that acute parenchymatous nephritis occurs in the secondary stage of the acquired disease. As such it can only be regarded as one of the symptoms of the general infection. It is the type of nephritic disease which occurs when syphilis is unsuspected as a cause that I shall discuss here.

That syphilis is a factor in causing chronic Bright's disease is almost completely disregarded in most text-books. I do not mean to assert that syphilis is the cause of every case of Bright's, but I do assert (and I am confident that my assertion can be proven by established facts) that in a considerable percentage of cases it is the cause *per se* of this condition. As Rathery very aptly remarks, "It is often very difficult to estimate the part taken by syphilis in the development of renal lesions. An old syphilitic affected with

Bright's disease often carries a more or less heavy etiological baggage (scarlatina, influenza, typhoid, lead, gout, etc.) and it is not easy to unravel what is due to syphilis." It has long been established that granular kidney is very frequently encountered in general paralysis of the insane which we know to be absolutely of syphilitic origin. Karvonen tabulated a large number of cases of nephritis in syphilitics. He proves that in many instances, contrary to generally accepted opinion, many of these cases were distinctly benefited by antisyphilitic treatment. My own experience has been similar. Nephritis developing during syphilis and due thereto is never injured in my opinion by either arsenic or mercury, but on the contrary the symptoms clear up under its influence. I am borne out in this by Gubler who states: "When a patient shows all the symptoms of a nephritis, either acute or chronic, and the etiology is doubtful, it is necessary to think of the possibility of syphilis."

Gummata of the kidneys are of very rare occurrence, although upon autopsy in syphilitics healed cicatrices would seem to indicate that they had occurred. Virchow found such evidences which he regarded as due to absorbed syphilomata.

Addison's Disease and Syphilis.—A disease of metabolism which I believe to be entirely due to syphilis is Addison's disease, the so-called bronze skinned disease or melasma suprarenalis. I am well aware that most pathologists ascribe this disease to a tuberculous infection of the capsule of the gland, but I think sufficient evidence can be produced to show that the Treponema pallidum is equally guilty in causing this strange malady. Long ago the late R. W. Taylor reported two cases which terminated fatally in which upon autopsy gummatous infiltration was found. Cases have also been reported by Sezary and also by Sacaze and Gordon. It has been observed by Fildes and McIntosh that the suprarenals are seemingly sites of predilection of the Treponema pallidum. As is to be supposed when a considerable number of the organisms are present there are well-marked histologic changes. The most striking features of these are small round-celled infiltration of the medulla, which in some instances is so severe that small necrotic areas are produced. There is also considerable hyperplasia of the connective tissue stroma which may be so excessive as to constitute an actual fibrosis. The treponemata are evenly distributed through the medulla and cortex with a preference for the epithelial cells and perivascular structures. Fordyce has also noted that in acquired syphilis amyloid degeneration is not uncommon. He has also noted a case of gummatous infiltration of the gland in which all of the classic symptoms of Addison's disease were present. The same has also been observed by Schaffner and Howard, and Levaditi found the treponemata present in large numbers both intracellular and

extracellular and he regarded that late heredosyphilis would account for many cases of the disease.

Diabetes and Syphilis.—Diabetes is a prevalent disease. There is no physician in general practice who does not come in contact with it. Its exact etiology has long been a matter of dispute both to pathologists and clinicians. We know that lesions of the fourth ventricle will produce it in dogs and it has also been asserted and proved beyond doubt that disease of the pancreas will also give rise to the condition. The lesions of the organs mentioned as causing the disease in many instances are due to syphilis. As long ago as 1907 Gaucher claimed that the material to prove the relation of diabetes to syphilis was constantly increasing. He stated that although it was usually a tertiary manifestation it could also occur as a symptom-complex of the secondary stage of lues. Von Noorden was also of the same opinion when he asserted that endarteritis of the pancreatic vessels would lead to glycosuria. In 1911 Camesatti reported a case of diabetes mellitus appearing ten years after a primary sore, with a positive Wassermann, which cleared up under the influence of mercury and potassium iodide. Futcher states that nutritonal changes in the brain and pancreas from syphilitic arterial disease must be considered as a possible cause of diabetes. In 10 per cent of his cases of paresis it was present, and Strauss reports it in 9 per cent. It would seem to me that if 10 per cent of paretics show glycosuria the relationship between syphilis and diabetes is not an occasional one. The occurrence of a positive Wassermann in a considerable number of diabetics and the apparent improvement following mercury and arsphenamine, and the association of glycosuria in children with congenital syphilis and the same condition in adults with paresis, tabes and other syphilitic affections have been reported in recent literature.

In 1916, Warthin and Wilson reported that since 1907 there have occurred in the autopsy service of the University of Michigan 6 autopsies on cases of diabetes. All 6 of these cases presented pathologic changes typical of syphilis, and in 4 of them the treponemata were demonstrated in the myocardium, and in 1 of these cases the treponemata were also found in the pancreatic lesions. When the pancreas of each of the 6 cases was given a more detailed study it was found that the pathologic changes were essentially the same in all, but varying in degree. These changes were as follows: (1) Atrophy with fatty infiltration involving particularly the tail and body of the organ; (2) increase of stroma, both interlobular and intralobular, particularly marked about the ducts and extending along the intralobular ducts between the acini and presenting the picture of a chronic interstitial inflammation, was shown in all 6 cases. These changes were most marked in the splenic end and

body of the organ. This increase of stroma was not uniform but occurred in patches, there being normal lobules side by side with lobules showing marked fibrosis. The lobules showing an increase of stroma were somewhat shrunken in size and also contained deposits of adipose tissue. Occasionally areas where the fibrosis was complete were found in the more severe cases; (3) inflammatory infiltrations, usually of small size, were found in every instance, both in the interlobular connective tissue and within the lobules as well. The cellular elements of this inflammatory process were almost entirely mononuclear, small and large lymphocytes and plasma cells. Polynuclear and eosinophiles were rare. The infiltration was loose and semi-fluid, resembling edematous tissue and contained epithelioid fibroblastic cells. It was these areas in which the colonies of treponemata were found.

Changes in the islands of Langerhans were present in all 6 cases. Changes were also shown in the acini. Occasionally acini with hyaline protoplasm staining deep red with eosin were found. Numerous structures looking not unlike newly formed islands were observed in the areas where the fibrosis and inflammation was most marked. Careful study showed them to be new-formed lobules of acini arising from the ducts.

To sum up, in these 6 cases an interstitial pancreatitis involving both the lobules and the acini, with more or less disappearance of the islands of Langerhans was shown. In all 6 syphilis was present in other organs as well. In 1 case treponemata were found in the pancreas itself proving absolutely the existence of a syphilitic pancreatitis as the cause of the diabetes. From the findings in the other 5 it is reasonable to assume that syphilis was the primary causative factor.

From the observations of the eminent pathologists it would seem possible that latent or occult syphilis is a most important factor in causing that form of pancreatic disease from which the symptom-complex of diabetes arises.

It is worthy of note that in diabetic gangrene the arteries supplying the affected part almost invariably show sclerotic changes, and it is well known that the Treponema pallidum shows a special predilection for the vascular system.

The relation of syphilis to diabetes has been extensively investigated by Troller. The conclusions he formulates are well worthy of consideration. They are as follows: (1) Diabetes should not be considered as a morbid entity, but as a syndrome of varied origin. Syphilis may be considered as a frequent cause of this syndrome. (2) Saccharine syphilitic diabetes may appear in secondary syphilis but is more common in the tertiary stage of the disease. (3) In secondary syphilis there is sometimes transient glycosuria which in

some cases may become true diabetes. (4) Glycosuria is due to disordered metabolism, while diabetes is caused by a cerebral lesion. In tertiary syphilis there are three forms: (*a*) Nervous diabetes, occurring in subjects from twenty to forty years of age, during the first four years of the disease and accompanied by cerebral phenomena. (*b*) Pancreatic diabetes, occurring from fifteen to twenty years after infection. This is of grave prognosis and is characterized by a fibrosis of the pancreas and a secondary affection of the islands of Langerhans. (*c*) Diabetes without cerebral or pancreatic symptoms, occurring in middle aged persons fifteen or twenty years after infection. This is of doubtful pathogenesis but is more amenable to treatment than the other forms. (5) Parasyphilitic diabetes may occur and is but slightly influenced by specific treatment. (6) In herodosyphilis diabetes may occur and is cured by mercury and arsphenamine. Considering the frequency of syphilitic pancreatitis in the subjects of heredosyphilis, this may be cited as a cause. (7) Syphilis may possibly explain the occurrence of conjugal diabetes.

Until quite recently the literature on diabetes, and it has been vast, contained nothing concerning the etiology of the disease except in a vague and general way, or else theories were advanced which later could not stand in the light of modern knowledge. The more recent pathologic studies of the disease, however, have led to the conclusion that the symptoms which taken collectively constitute the condition, are caused by some derangement of the pancreas, more especially by some derangement of the secretion of the islands of Langerhans. In my mind the preponderating evidence is in favor of the pancreatic origin of diabetes, except in those cases where there is undoubtedly a lesion of the fourth ventricle. The question then arises, what is the cause of this functional defect? Since we know that the immediate cause of diabetes is some interference with the proper oxidization of certain food elements, we have the most positive evidence that the appearance of sugar in the urine is caused by lesions in organs differing so greatly in structure and function as the brain and pancreas. Now, it is not improbable that some common cause which, owing to inherent or acquired weakness of one or the other of the organs mentioned—a *locus minoris resistentiæ* as it were—can so interfere with their normal functioning that the necessary oxidization is inhibited to a degree sufficient to induce the affection. This disturbing element which is responsible for very many cases of diabetes irrespective of the nature or location of the lesion to which organically it is most directly related—this common and most potent cause which we know can permeate every organ and tissue of the body and by its

blighting touch vitiate every secretion and derange every function is the Treponema pallidum.

The importance of this observation is not difficult to understand. It shows that many well defined conditions, erroneously supposed to be of obscure or unknown origin, are in reality the symptoms masked under the name of another affection, the origin and nature of which are thoroughly understood, and the removal of this underlying cause is in many instances well within the bounds of possibility.

Hyperthyroidism and Syphilis.—Hyperthyroidism, or as it is commonly termed Basedow's disease, is another symptom-complex usually regarded as of obscure etiology and which is also extremely rebellious to treatment that I believe can, in many instances, be traced to syphilis. It is well known that the thyroid is frequently involved both in acquired and hereditary syphilis. The literature on the subject is extremely scant but I think there is sufficient to show that in many instances a definite relationship exists between syphilis and the symptom-complex generally known as Basedow's disease.

Cases of this disease in which the underlying causative factor was undoubtedly syphilitic have been noted by various observers. Poncet and Leriche have reported a case in a woman with syphilis who developed symptoms of hyperthyroidism and who was cured by arsphenamine. Thompson has recorded a case of hyperthyroidism in a man aged seventy-two years, who showed a pulse rate of 140, with protruding eyeballs. This patient had a gumma of the thyroid. Under antisyphilitic treatment the symptoms disappeared. Similar cases have also been reported by Hazen, Montgomery, Lockwood, Gombault and Pospelow.

The limits of this chapter will not permit a continued discussion of all the diseases in which syphilis can in many instances be regarded as a causative factor. That it is a factor and a most potent one in a wide variety of ailments cannot be denied. I have only touched upon a few—a very few, I may say. Syphilis should always be looked for and, if found, treated. A disease so insidious, so protean and so widespread as syphilis cannot but be regarded as a cause in all diseases which are chronic or which are out of the ordinary.

CHAPTER XXX.

SYPHILIS AND MALIGNANT DISEASE.

The lesions of syphilis are not infrequently mistaken for malignant disease, and the contrary is also true. The study of any relationship, that may exist between them is therefore of absorbing interest.

The cause of syphilis we know; the cause of cancer is still a mystery. The two disease have been observed for many centuries and the pathology and clinical phenomena of each are well defined. Yet, from time to time we cross a border line where the two dyscrasias seem to meet and merge, and where are secrets still unsolved. It is our purpose, therefore, in this chapter to examine these clinical enigmas and to look for any relation which may exist between the two.

Ancient View.—The oldest view regarding the relation which was supposed to exist between malignancy and lues was that they were mutually antagonistic to each other. Some even went to the extreme and insisted that a syphilitic was immune to cancer. As is frequently the case where only theories are concerned the pendulum after a while swung in the opposite direction. The affirmative was unqualifiedly given to the question—"Does syphilis increase the predisposition to malignant disease?" Among syphilologists and, to a certain extent, amongst surgeons as well, this now the consensus of opinion. Let us proceed to examine the reasons why this view is held.

More Recent Views.—As far back as 1843, Leroy d'Etiolles stated that one syphilitic out of twenty-five developed carcinoma—that is, 4 per cent. In 1884, Ozenne put forward the opinion that syphilis determined the point of least resistance for the appearance of carcinoma. In 1888, Cozzoline produced evidence of a conclusive nature that cancer developed rapidly on a background of early syphilis and more slowly on late syphilis. He also stated that when cancer appeared on what had formerly been a syphilitic lesion it was accompanied by a relapse of the luetic infection. Esmarch, and Wasmer, advanced the postulate that because of the tendency of syphilis to attack connective tissue, the presence of lues would favor the development of sarcoma rather than carcinoma. In a paper published in France just before the war, Poirier reported 32 cases of malignant disease of the tongue in which 27 were syphilitic.

The German surgeon Dieffenbach was so thoroughly convinced of the fact that malignancy follows syphilis that after every operation for the removal or amelioration of a cancerous growth he instituted a course of mercurial inunctions.

Pelvic gummata are lesions concerning which there is scant mention in the literature, yet they cause a form of pelvic cellulitis which is of extreme interest to the surgeon, in that they may closely resemble sarcoma or carcinoma both clinically and by the *x*-ray as well. In this connection a case mentioned by the younger Fournier is of more than passing interest. The patient was a man, thirty-four years of age, upon whom had been made the diagnosis of inoperable sarcoma. There was marked cachexia and pelvic infiltration of boardlike hardness. The glands were not enlarged. There were no evidences clinically of syphilis except upon ocular examination. This was before the days of the Wassermann test so that the serologic state was not ascertained. As a last hope, as it were, Fournier instituted a course of mixed treatment. The patient recovered.

Cancer Occurring in Scar Tissue.—It is well known clinically that carcinoma or epithelioma not infrequently occurs on the site of a healed syphilitic scar. But it must also be remembered that cancer occurs with equal frequency on scars which are not of syphilitic origin. So eminent an observer as Jonathan Hutchinson stated that he had often seen a malignant growth developed on a healed syphilitic lesion. Czerny and Caan, in the Heidelberg Cancer Institute, took a Wassermann of all cancer patients admitted thereto and were surprised to note the frequency of positive reactions. Salvarsan had no effect in so far as carcinoma or epithelioma was concerned, but with sarcomatous growths they sometimes obtained favorable results. It has also been observed in the so-called Dithmar disease, which we now know to be a form of inveterate hereditary syphilis, that many of those so affected subsequently developed malignant disease. It not infrequently happens that gastro-enterologists encounter palpable tumor masses either at the cardiac or pyloric orifice of the stomach which are extremely difficult to diagnose from malignant growths (see Chapter XL). In many of these cases cachexia is marked and the gastric symptoms closely simulate those of carcinoma of the stomach. It is needless to state that these "carcinomas" rapidly disappear under antiluetic treatment.

Syphilis or Cancer of the Tongue.—In 1907, Horand in an extensive review reaffirmed the postulate that syphilis is a predisposing factor in causing malignancy. He reported at length 168 case histories, most of which referred to cancer of the mouth or tongue. Nearly all of them had leucoplakia lingualis or buccalis previous to the

development of malignancy. Now the consensus of opinion amongst syphililogists is that leucoplakia is due to syphilis. Personally I have never seen a case that did not have a positive Wassermann. Fournier asserts that leucoplakia is invariably syphilitic, and Berenger, Kopp, Kaposi, Landouzy and Gaucher also regard syphilis as the sole cause of leucoplakia. Fournier further states that many of these cases later become malignant. In support of this statement he cites the analysis of 184 cases of buccal cancer following leucoplakia in which 84 per cent were known to have had syphilis. I have already mentioned Poirier's series of cancer of the tongue of which 27 out of 32 were syphilitic. It must be admitted that such frequent occurrences cannot be due to coincidence. I desire, however, to call the reader's attention to the fact that these cases occurred almost entirely in males, and many of them gave a history of prolonged and excessive use of tobacco, so that a diagnosis of smoker's cancer would not be entirely out of place. The French dermatologist, Brault, writing in 1898, claimed that in epithelioma of the tongue there was almost always a history of syphilis in youth. This was before the days of the Wassermann and it is quite possible that Brault was mistaken in some of his cases of epithelioma which were really syphilis.

Juxtasyphilitic Cancer.—In the series reported by Horand he notes that 40 of them were of a hybrid type; *i. e.*, cancer and syphilis were present in the same lesion. He calls these juxtasyphilitic cancer. Case L, in his series, illustrates this condition very well. A man of thirty-eight had an infiltrated ulcer of the lower lip which had persisted for a long time, but which yielded promptly to potassium iodide. After two years the ulcer returned, when it was found to be cancer in part; that is, syphiloma with cancer nests. I am reminded of a similar case brought to my attention at autopsy in which there were lesions on the buccal and lingual surfaces and larynx that were patently syphilitic, yet histologic examination demonstrated that a transformation into epithelioma was taking place. Cases such as these are not uncommon, but as Horand gathered his data before the discovery of the Treponema pallidum and the Wassermann reaction, it is quite possible that the knowledge we now possess would, in some instances, have modified his diagnosis. Similar cases of malignant growths grafted upon gummata have been reported by Jaboulaye, by Montgomery and Sherman, and by Rohrbach, pathologist in the University of Breslau. I am of the opinion that they represent a true clinical entity and Horand and Fournier were undoubtedly right in classifying some of them as hybrids—carcinoma or epithelioma coexistent with syphiloma in the same lesion.

Cancer and Chancre.—As the penis is the most frequent site of chancre, it is of interest to note the number of malignant growths originating upon that organ in which there was a previous history of syphilis. In 1877, Demarquay collected 134 cases from the literature and from personal experience. In 59 of these syphilis is given as the cause. His paper is somewhat lacking in detail, but the inference he draws is that chancre, chancre redux, and gummata have a tendency to cause cancer. In an analysis by Downey of 100 cases of epithelioma of the penis occurring in the Massachusetts General Hospital from 1872 to 1905, he notes that in 2 the cancer appeared on the site of the chancre after a lapse of twenty-two and thirty years, respectively, Martin and Sibley also report having seen a cancer develop on the former site of a chancre. Some two years ago I saw a cancer of the penis in a patient of middle age who gave a history of having had a chancre twenty years before. The Wassermann was strongly positive in spite of vigorous treatment with arsenic and mercury.

King, of Kansas City, writing in 1898, described a number of cases of syphilis which had apparently been contracted from individuals suffering with cancer. It so happened that nearly all of the victims of the syphilitic infection were surgeons who had developed digital chancres after operating on cancer. In none of them was there any doubt of the diagnosis of syphilis in the patients operated upon. King, however, fails to state whether any of these cancerous patients showed any of the clinical signs of lues. Also he wrote before the discovery of the Treponema pallidum and the Wassermann reaction and his method of bacteriologic expression, if I may be allowed to use that term, is not altogether in accord with modern ideas. Yet, however we may speculate, the fact remains that four surgeons were inoculated with syphilis while operating on cancer; which proves at least, that these four cancer cases were also actively syphilitic.

Simulation of Cancer by Syphilis.—Coming nearer to the present and within the period of the Wassermann and the Treponema pallidum, let us consider the two diseases from the angle with which they have been studied by O'Day—the exact simulation of cancer by syphilis. O'Day describes a case which may be taken as typical: A woman, aged forty-eight years, who had been examined by a number of competent men and her condition diagnosed as cancer of the cervix. The odor characteristic of uterine cancer was present and she had metrorrhagia to an extent to render her extremely anemic. She was cachectic and also had bed sores. Suddenly mucous patches appeared. A Wassermann was taken which was found to be strongly positive. Under antisyphilitic treatment the patient recovered. O'Day enumerates several other cases of sup-

posed malignancy which in reality were syphilis; one that had been diagnosed as cancer of the stomach, another of an intra-abdominal growth and one of a growth involving the orbit.

Syphilis a Cause of Malignancy.—I have no hesitation in saying that I believe syphilis to be a factor—a very potent factor—in the causation of malignancy. In this opinion it may be seen that I am not alone. Especially is this true in regard to buccal and lingual cancers which form a not inconsiderable percentage of malignant disease. I believe that this causal relation exists between them because syphilis produces a *locus minoris resistentiæ* that renders the tissues more susceptible to the development of aberrant cells. I am also of the opinion that in every case of supposed malignancy, careful exclusion of syphilis should be made. This advice, however, should not be taken too literally. To disregard this sometimes leads to results that are not satisfactory. Especially is this true in the domain of surgery. To differentiate between syphilitic growths and neoplasms of other origin often taxes the skill of the most experienced. In regard to bony growths, the *x*-ray will often enable a certain decision to be made, but in the soft parts this help is not always afforded. It is the part of wisdom, therefore, in these cases not to depend entirely upon the Wassermann. For it is quite possible, as I believe I have shown, for the two conditions to exist side by side, and yet be independent of each other. In these confusing cases I strongly advise the use of the therapeutic test; that is, a week or two of the vigorous antisyphilitic treatment if circumstances so allow, but it should be carried no further if no results are shown.

In conclusion, I am convinced that it is undoubtedly proven that syphilis predisposes to malignant disease; that the most malignant forms of syphilis and cancer can exist side by side—the so-called juxtasyphilitic carcinoma or epithelioma. In a syphilitic developing malignant disease there is almost certain to be a local outbreak of the luetic disease in close proximity to the malignant growth. In an individual with cancer who contracts syphilis the malignant disease is stimulated to increased activity. Epithelioma or carcinoma may develop on a gumma, the two lesions merging, as it were. Syphilis may exactly simulate cancer in any location, either in the viscera or on the surface of the body.

CHAPTER XXXI.

PARESIS.

Paresis is an inflammatory, degenerative meningo-encephalitis characterized by systemic physical symptoms and progressive mental deterioration due to the localization of the Treponema pallidum in the cerebral tissues.

Pathology.—The pathology of paresis, macroscopic and microscopic, indicates the profound changes that have taken place in the brain. Similar, although much less extensive changes, can however occur in senile arteriosclerosis and the chronic leptomeningitis caused by chronic and inveterate alcoholism. The dura is markedly thickened, due to an extensive round-celled infiltration; it is usually adherent to the calvarium and in most instances shows evidence of either widespread or isolated hemorrhages. This hemorrhagic pachymeningitis is sometimes found in other conditions than paresis. The pia arachnoid is thickened and opaque or else it is edematous; the thickening and cloudiness being especially noticeable along the course of the bloodvessels. These alterations of the pia arachnoid are found over the anterior and middle portions of the frontal lobes. They do not extend posteriorly. The Pacchionian bodies are usually enlarged but the cortex is atrophic and the convolutions are shrunken and in these depressions over which the membrane is stretched is found a collection of turbid serum. The cortical atrophy causes a considerable loss in the weight of the brain —from 100 to 130 gm. The ventricles are dilated and the ependyma is coarsely granular. This granular appearance also occurs in other conditions than paresis.

The microscopic changes in the brain in paresis consist of a diffuse inflammatory degenerative process. The indications of inflammation are infiltration of the meninges and the adventitial lymph spaces. This infiltration is more extensive in the cerebrum but it is also more or less present in the cerebellum, the deep structure of the brain and the spinal cord. The cerebral cortex is the part most infiltrated. The infiltration is also particularly noticeable about the lymph sheaths and the delicate cortical vessels and in this respect is characteristic of paresis. The cortical nerve cells show all stages of degeneration and many of them disappear entirely. The protoplasmic prolongations of the cells are lost as are also

medullated fibers. There is a glial overgrowth on the free border of the cortex which later extends downward and upward and also surrounds the bloodvessels. Degenerative changes in the gan-

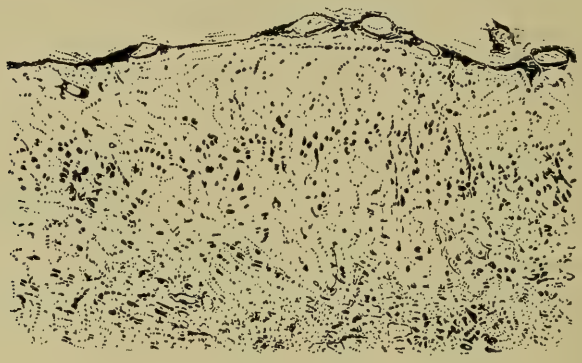


FIG. 64.—Cortex cerebri in paresis.

glionic cells also occur. These include disappearance of the chromatic granules and the nucleus, atrophy and pigmentation. While this destruction of ganglionic cells may be complete it is not always so and may be confined to a more or less limited area.

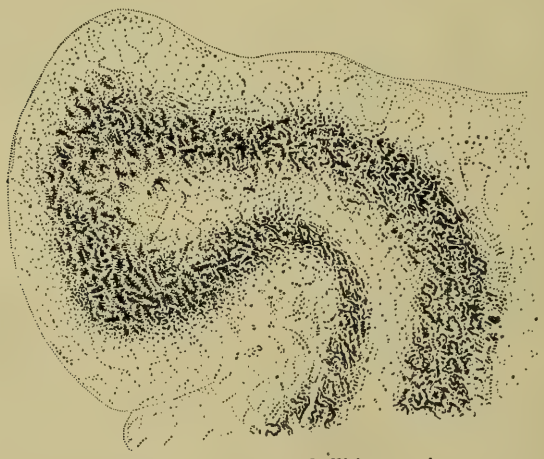


FIG. 65.—Cortex cerebelli in paresis.

The lesions just described are mostly confined to the cortex of the cerebrum but the cerebellum and spinal cord are also involved. Degeneration of the ganglion cells and of the optic nuclei explain

the eye changes observed in paresis. The changes in the optic thalamus and the cerebellum consist mostly in neuroglial proliferation.

Etiology.—The Treponema pallidum was first demonstrated in paretic brains by Noguchi and Moore in 1911; the organisms being scattered through the cerebral substance in no particular relation to the vessels. Thus was verified what had been long suspected that paresis was caused by syphilis. To ascribe it to other causes as is still done occasionally is to display an ignorance and a lack of knowledge of the established facts that are inexcusable at the present time. So too is the idea entertained by a large number of the laity that unnatural sexual practices, especially buccal coitus, causes paresis. Paresis is due to syphilis—it is a phase of syphilis—the last, the most horrible of all. For, in its full development it is the sum of horrors with death a sweet nepenthe. It is said to be a comparatively modern disease. It is not mentioned in the medical writings of the eighteenth century or before. Even a hundred years ago it was a medical curiosity. Not until the middle of the last century did it begin to attract attention by its increasing frequency. The disease is most frequently encountered among the higher intellectual types—the brain workers and executives, rather than among those who earn their bread by the sweat of their brows—mechanics and manual laborers. Alcohol, mental exertion and emotional strain, sexual excesses are mentioned as predisposing causes, but not in every instance. Some syphilologists have expressed the formula "Syphilis plus alcohol equals paresis." While undoubtedly true in some cases it is by no means true in all. Hazen has called attention to the fact that paresis can occur in total abstainers. The theory, recently advanced and which has become quite popular, that a special or neurotropic strain of Treponema pallidum causes paresis and other nervous manifestations I believe to be incorrect. I am convinced that no such strain exists. The development or non-development of paresis or any other form of nervous syphilis, is, in my opinion, entirely a question of *locus minoris resistentiæ.*

Prevalence.—Paresis is comparatively rare among uncivilized peoples although among them it must at times undoubtedly occur. Kraepelin also calls attention to the extraordinary and inexplicable differences in the incidence of the disease in different countries. In France, England, Germany, Austria, Italy, Switzerland, Holland, Belgium, western Russia and the eastern part of the United States the percentage of syphilitics who develop paresis is practically the same, but in Spain which is also a country of western Europe the disease is much less frequently met with. It is also less frequent in Sicily than it is in northern Italy and it is more frequent in

Scotland than it is in Ireland. In Norway it is of extreme rarity—some institutions for the insane frequently not having admitted a case for years. It is equally rare in Iceland. In the Balkan states it is also comparatively rare. Among the natives of the Mediterranean littoral of Africa it is rare, but among the Europeanized Arabs of Cairo and Alexandria it is by no means infrequent. The same is also true of the Europeanized Algerians. The Turks however, are little inclined to the disease as are also the Levantine Jews. Among the uncivilized blacks of Africa it is apparently unknown. It is also only rarely encountered in Asia Minor, British India, Siam, Polynesia and other backward civilizations. In Japan however, it is now as prevalent as among the western nations.

One is inclined to attribute the differences of incidence to racial peculiarities, because in all of these countries the white representatives of the western civilizations show no diminution in susceptibility. This is further exemplified by the fact that in Constantinople the disease is more prevalent among the Greeks and Armenians than it is among the Turks. In Cuba the blacks are much less affected than the whites, and in Brazil it is almost unknown among the native Indian population while it is present among the white element. In a general way we may say that racially the disease is more frequent among the Slavs, Teutons—including the Anglo-Saxons—and the Latins; it is less frequent among the Celts, Semites, Mongolians, Indians, Negroes and Polynesians. It would seem therefore, that a causal relation exists between the habits of life, the degree of civilization and, most of all in my opinion, the length of time syphilis has been endemic. The disease is more frequent in men than in women, although in the last few decades the proportion between them seems to be gradually lessening.

Osnato has called attention to the question, that has long been an unsolved problem to psychiatrists and syphilologists, why is it that while so large a number of people contract syphilis yet of these, so few comparatively—not more than 2 per cent—ever develop paresis. His explanation (and with him I am in accord) is that if we postulate in these patients a defect in the nervous system existing as an hereditary weakness the question is in part at least perhaps explained by Adler's conception of organic inferiority. Adler believes that the neurotic or psychopath is somatically inferior, and therefore if we can prove that before the development of the psychosis the paretic was a neurotic or psychopath, we can say that the process developed because the central nervous system was the *locus minoris resistentiæ*. Osnato is of the opinion that paresis is more apt to occur in persons with abnormal personalities, *i. e.*, those of unstable mental equilibrium or those with a hereditary

degenerative tendency. The Treponema pallidum we know has a decided predilection for the tissues which combine to form the nervous system and when to this is offered the lessened resistance of a nervous system congenitally weak it is only logical to infer that it will bear the brunt of the syphilitic attack.

Of late the theory has been advanced and it has found many adherents, that neural syphilis is a question of a particular strain of treponema which is neurotropic to the nervous system. Some observers have even gone so far as to describe in detail the morphologic features of this neurotropic strain of the organism of syphilis. The additional arguments also include the relation of cases of conjugal paresis and tabes, as if these two syndromes were the only nervous lesions produced by syphilis. That there is a strain of treponema which produces nervous lesions to the exclusion of others I utterly deny.

Paresis is said to be the slowest evoluting disease known. From the clinical and somatic standpoint this statement may be challenged, but from the point of time when the infection is manifest in the cerebrospinal fluid I believe it to be true. The involvement of the nervous system in syphilis is in many instances practically synchronous with the appearance of the initial lesion. There is ample evidence of this. The researches of Dreyfus, Leishman, Ravaut, Fordyce and others have shown that the specific reaction of syphilis is present in the cerebrospinal fluid of from 20 to 35 per cent of all syphilitics examined in the first year of the disease. Wile and Halsey found deviations from the normal including a positive Wassermann reaction in 49 out of 221 cases of syphilis in which only the chancre was present. Thus it will be seen how quickly syphilis attacks the nervous system. If we strike an average of the percentages noted by the various observers it can be assumed that fully one-fourth of all syphilitics in the first year of the infection will show an invasion of the cerebrospinal axis. This invasion is independent of any nervous lesion being manifest. Therefore it cannot be denied that any person with a positive Wassermann reaction or other abnormal findings in the spinal fluid is, perforce, a potential neuro-syphilitic, which may take the form of tabes or paresis or any of the other forms whereby nervous syphilis is exhibited. However, in by far the majority of instances this early involvement either resolves spontaneously or as the result of treatment. A certain percentage of them do not. Some of them—approximately 1 or 2 per cent—eventually develop paresis. As to why they do so I have already stated my opinion.

Cerebrospinal Fluid.—An account of the changes in the cerebrospinal fluid are of the utmost importance in the study of paresis. I cannot emphasize too strongly the need of a cytological examina-

tion of this fluid in all suspected cases. It simply must be done; otherwise the physician does not do justice to himself or to his patient. In paresis the fluid flows from the needle under greatly increased pressure. This, however, may occur in other conditions. The cell count is always increased and this is invariable except shortly before death from the process. The cellular elements are mostly small leukocytes. The amount of globulin is increased, but this increase can occur in other conditions and therefore is not in itself pathognomonic. In the earlier stages there is a reduction of Fehling's solution but when the disease is well advanced this reduction does not take place. Lange's colloidal-gold test will usually, although by no means always, show the so-called paretic curve. Quite a number of syphilologists and neurologists place great stress on this test as evidenced by the presence or absence of the curve. Personally, while willing to concede its weight, I think its importance has been unduly exalted. The Wassermann reaction is always positive in paresis even with extremely small amounts of fluid. This is most important in diagnosis because with small amounts a positive reaction is not often obtained in other forms of nervous syphilis, but in paresis it never fails to be returned positive. *If it is negative it is not paresis.* The blood is also positive in paresis. *If it is negative and the spinal fluid is positive it is not paresis. A positive serum and a positive spinal fluid are always present in paresis.* These two facts should always be borne in mind because they never vary. Also, unless in the very earliest stage, no matter how much treatment the patient receives, the spinal fluid always remains positive to the Wassermann reaction in paresis.

Prodromal Symptoms.—If it were possible to examine the cerebrospinal fluid from the first year of the syphilitic infection and, let us say, every year thereafter, it might be possible to determine just when the paretic process began, but since this is not possible we must depend upon the clinical signs alone, and these are not noticed until the prodromal stage is reached which is usually about five years before the somatic and character changes are sufficiently marked to enable a diagnosis to be made. Even after this lapse of time the diagnosis is in many instances tentative unless confirmed by the Wassermann test of the blood and spinal fluid. The prodrome which must frequently precedes paresis is neurasthenia. A neurasthenia arising from a cause which cannot be absolutely determined in a person between forty and fifty years of age, especially if the patient admits syphilis or whose blood is positive to the Wassermann test should receive careful consideration as to the possibility of a developing paresis. This neurasthenia frequently assumes the form of a mild anxiety neurosis with only slight character changes. These changes are irritability, trifling memory defects

and some loss of efficiency in the work the patient is capable of, or in the habit of, doing. The patient may also complain of headache and insomnia, the headache, however, is not as violent as in cerebral syphilis. There may also be dysesthesia and paresthesia, but these sense abnormalities are not usually marked. At this early stage the reflexes, including those of the pupils, are normal or only slightly exaggerated; also, the patient's mind is perfectly clear.

At this stage treatment may arrest the progress of the disease. It is the patient's hour of fate; for, if neglected because of lack of forethought on the part of the patient, or because of a faulty diagnosis on the part of the physician he is doomed. Nothing can save him. Very rarely the disease may progress until the pupillary and the ankle and knee reflexes are lost and then remain stationary spontaneously or through treatment. Within, and only within, the limitations mentioned, I am in accord with Dana that paresis is curable, or it is at least possible to obtain a long remission. Otherwise the psychic changes slowly increase and gradually become sufficiently noticeable to cause apprehension on the part of the patient's relatives and friends.

The Convulsion.—The prodromal stage is usually closed by a convulsion or "stroke." This is the most striking motor feature of paresis and it occurs in the majority of cases, although the percentage is estimated according to various observers to range between 30 and 90 per cent. They are probably due to an acute congestion or a circumscribed edema of the cortex. The convulsion may simulate apoplexy very closely but with the difference that the paralysis consequent thereto usually clears up much more quickly and completely than when the apoplexy is due to some other cause. It will also be noted, which is most important, that while the paralysis may soon disappear or nearly disappear, the patient's intellect is *never* as good as it was before. With each succeeding attack, and these attacks are invariably followed by others, the intellect steadily deteriorates.

Psychical Changes.—Sooner or later the changes in the intelligence, the judgment and moral character are patent to all. The patient's conduct and attitude toward life undergoes a complete *volte face*. It is this change which accounts for the "fall from grace" of many otherwise good men. The model husband and father seeks the society of immoral women and thereby causes much scandal which cannot be explained. The pious and circumspect may utter oaths and obscenity and seek the companionship of those far beneath them. The shrewd man of business may engage in ventures that entail much loss financially. Again, strange to say, so completely does the disease twist and turn the character about, the licentious libertine may, unlike the leopard and his spots or the Ethiopian and his

skin, change his ways and follow—when it is too late—the straight and narrow path.

These patients are boastful; they laugh loudly at their own jokes, no matter how poor or inappropriate they may be. They are very open to suggestion and flit from one subject to another with startling rapidity. They are subject to sudden change of moods, from laughter to tears and from tears to laughter. Yet, all the while the patient may be mingling in the world and attending to his daily affairs—after a fashion. Not infrequently remissions occur and the patient may seem much improved. If the psychosis has progressed so far that he has been confined to an asylum he may even be able to return home and resume his former place in life but never, let it be remembered, with anything like his former vigor. These periods of remission are usually terminated with a convulsion and from this the patient may recover somewhat, but after each, as I have already stated, the improvement does not reach the same level as before—the tendency is constantly downward. There is now to be noted a gradual loss of acquired knowledge, although those facts with which the patient is most familiar, such as his daily routine of work, are retained the longest. Thus the engineer will retain his special knowledge of mathematics even when quite far advanced in his psychosis. It is only a question of time however, when even this knowledge is lost and as the amentia develops the patient may outrage all of the proprieties; he may attend to the calls of Nature without any regard whatsoever to his surroundings, or masturbate or make indecent exposures regardless of time or place or circumstance.

Final Stage.—The final stage finds the patient a bed-ridden paralytic. The mind is completely gone, only the body lives—precariously. Unless carefully attended, bed-sores develop which may attain huge proportions. The bones fracture and the teeth fall out, due in all probability to trophic changes. The emaciation is extreme. There is obstinate constipation. Asthenia, myocarditis, nephritis or pneumonia closes the scene which from the end of the prodromal stage until then is rarely more than three years.

The sexual strength is frequently increased in the early stages of the disease and this probably accounts for the moral lapses committed by so many of these patients in that stage. Later there is complete impotence. Herpes following the course of some of the cranial or spinal nerves is sometimes seen. Disturbances of the bladder, such as incontinence or nocturnal enuresis are also observed early in the disease. Later the bladder sphincters are completely paralyzed and the patient voids spontaneously. If the process in the brain is complicated with a similar one in the cord—tabo-paresis—there may be vesical, gastric, laryngeal or rectal crises. In not a

few cases a coarse tremor is observed which may closely resemble Huntington's chorea. The organs of sense are frequently affected as the disease progresses and there may be deafness, loss of the sense of smell and of the sense of pain so that the patient may receive blows, cuts or burns without experiencing any pain therefrom. The viscera also seem to share this hypalgesia, whether due to trophic changes in them or to the mental hebetude it is not possible to say; probably the last. These patients may suffer from severe disease of the stomach, liver, or fractured bones without evincing any discomfort whatsoever.

Reflexes.—When the disease is established disturbance of the reflexes is invariably observed. Irregularity of the pupillary reflex is an early and practically pathognomonic sign. There is the miotic Argyll-Robertson pupils in which the light reflex is more frequently lost than the accommodation reflex. The reverse of this sometimes occurs in which the light reflex is retained but that of accommodation is lost. Instead of being miotic the pupils may be widely dilated or, one may be dilated and the other miotic. The pupils may be irregular, or excentric, that is, elliptical or flattened. In the early stage of the disease the reflexes of the ankle, knee, jaw, elbow and wrist are usually exaggerated. Later they disappear entirely. Those of the knee or ankle may be present on one side and absent on the other. Toward the end of the disease muscular rigidity and contracture are frequent. These contractures may be most severe and involve the entire musculature of the body. As they usually occur in the bed-ridden stage they frequently give a characteristic posture to the body as it reclines upon the bed.

In the early stage of the disease there is often a loss of weight, but later this loss is usually regained and the patient may even become obese; toward the end, however, the emaciation is marked. In the early stage the appetite is frequently diminished but as the disease progresses and the intellect deteriorates this may give place to bulimia and there may also be an appetite for strange and repulsive kinds of food. There is no change in the temperature in paresis except at the terminal stage, when, as would be expected, it is frequently subnormal.

There is something characteristic about the facies and carriage of the paretic which the skilled observer can often note before the condition is even suspected by the patient's friends. The countenance lacks expression. It is like a mask. There is a flattening of the nasal and nasolabial folds. It sometimes happens that one side of the face only is flattened. With this immobility of expression fibrillary tremors of the facial muscles are frequently observed. Inability to make several expressive movements in succession, like opening the mouth and protruding the tongue and wrinkling the

forehead are to be observed. The tongue trembles when protruded; there is a tremor of the hands. The voice changes. Quite early the tonal and inflective qualities are lost and it becomes a monotone, which once heard is not easy to forget. Owing to a paralysis of the vocal cords the pronunciation of some words becomes difficult and the speech becomes slurred. This fact is elucidated by asking the patient to repeat certain phrases, such as, "Irish artillery," "eleemosynary institutions," "British Constitution," "The rascal king ran 'round the rock." The handwriting also undergoes a change, and presents irregularities which may be compared with the speech defects. Letters, syllables and words are misplaced, repeated or omitted. Little or no attention is paid to spacing and sentences are frequently abruptly terminated at the end of the line. In well advanced cases the patient may make an attempt at writing but after a few futile efforts he usually gives it up with some trivial or ridiculous excuse.

All of the voluntary muscles sooner or later display a lack of coördination which is manifest by an increasing clumsiness in the performance of ordinary acts such as buttoning the clothes. Later, complicated acts become impossible. The general carriage becomes lax and later the gait becomes either shuffling or spastic—the last if the cord is involved.

In most of these patients there is an appearance of presenility. The hair is prematurely gray; baldness is common. The skin is wrinkled and sallow. There is an unkemptness about them that shows that the mind is no longer activating with its former precision.

Juvenile paresis I have discussed elsewhere and the reader is referred to that part of the book wherein it is contained.

Treatment.—Should the paretic be treated, and if treated can he be cured? I have already answered this question in part earlier in the chapter, but in order to make myself perfectly clear it may be well for me to answer the question plainly and unequivocally again. In the prodromal stage it is possible I believe to cure paresis if the treatment is carried out energetically and intelligently. When the process has advanced to the second or paretic stage treatment, no matter how skillfully or boldly given, is of no avail in so far as an ultimate cure is concerned. It is possible however, by treatment at this stage to obtain a remission of considerable length in some instances. When encephalomalacia is definitely established curative treatment should not be employed. It is useless. To make the patient comfortable is all that should be attempted.

I do not know what the future will bring forth, but once paresis is verified the patient's hour has struck and he is doomed. Naught that we now know can avail to stop this, the most terrible of all the protean forms of syphilis.

CHAPTER XXXII.

TABES DORSALIS.

Tabes dorsalis, or as it is also called, locomotor ataxia, is an organic disease of the peripheral sensory neurone system due to a primary, progressive degeneration of the same caused by the Treponema pallidum; it is characterized by symptoms resulting from disturbances of the sensory apparatus which are partly irritative and partly paralytic.

Changes in the Spinal Cord.—If the patient dies before the disease is advanced it is difficult to determine by the unaided eye any macroscopic changes at necropsy. If the disease is advanced, however, the spinal cord with its posterior nerve roots will show characteristic changes which can be so determined, and which require the microscope only for the determination of the finer details. The pia arachnoid between the two posterior horns is thickened, opaque and adherent to the cord. It has the appearance of a narrow, ribbon-like band extending the whole length of the cord. The posterior columns are shrunken and the dorsal roots are gray and atrophied. On section the dorsal columns appear gray and translucent in comparison to the pinkish, opaque white matter. This change cannot always be observed by the naked eye but when stained and examined under the microscope the distribution of the gray matter in the dorsal columns is plainly visible. This grayish translucence is due to the disappearance of the lipoid myeline sheaths and of the axis cylinders of the nerve fibers which are replaced by connective tissue.

Microscopically the sensory nerve roots show degenerative changes. At the beginning these changes are confined to the lumbar region and only a few roots and fibers are affected. Later other regions and many more roots and fibers are involved. The zone of Lissauer which extends across the entering fibers of the posterior roots shows early degenerative changes as does also the column of Burdach which borders on the posterior horns. The column of Clarke in the gray matter and the column of Goll and Gower's tract also show degenerative changes. It is these tracts which are concerned with the muscle sense and with the reflex arcs. It can be readily appreciated therefore, how any interference with them can give rise to the sensory and tactile disturbances which are

predominant in tabes. In the medulla the cells of the nucleus gracilis and the nucleus cuneatus are sometimes, but not always,

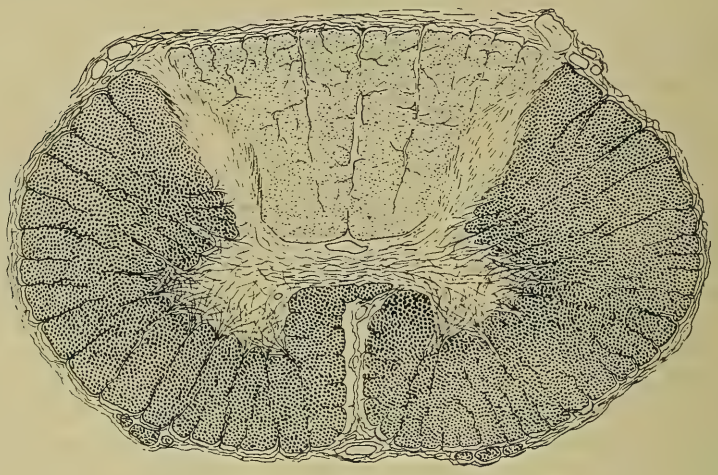


Fig. 66.—Tabes dorsalis.

Fig. 67.—Tabes dorsalis.

affected. Degeneration of the cells of the anterior horns are also observed. It is the changes occurring here which probably give

rise to the "crises" and trophic disturbances sometimes observed during the course of the disease.

Changes in Nerves.—As tabes is a disease of the peripheral sensory neurone system any or all parts of the system may be involved. Coincident with the degeneration in the cord similar changes are to be observed in the peripheral nerves; these changes are, however, confined chiefly to the smaller peripheral branches, and limited to the motor fibers exclusively. Among those included and which cause symptoms in many instances characteristic of the disease are the optic, auditory, pneumogastric, glossopharyngeal and trigeminal nerves. Degenerative changes are also observed in the spinal and cranial ganglia. The ganglion cells are reduced in size and number. Remotely removed from these are the degenerative changes to be observed in the sensory nerve endings of the skin, joints and muscles.

This widespread neuronic cellular degeneration, as in chronic syphilitic processes elsewhere, is replaced by connective tissue elements which are later transformed into more or less condensed fibrillar tissue; but even so, a few normal fibers invariably remain even when the process is far advanced. In the degenerated areas deposits of fat globules and amylaceous changes are sometimes observed. The bloodvessels which furnish the immediate blood supply of the cord show evidences of endarteritis.

Pathogenesis.—The real pathogenesis of tabes is still to be written. While we know absolutely that it is due to syphilis the exact mechanism whereby the primary neuronic degeneration is brought about is still a matter of conjecture. The earliest view, and one which is still held by many pathologists and syphilologists, is that it is caused by vascular obstruction, *i. e.*, a syphilitic endarteritis of the terminal bloodvessels of the cord. This theory was first advanced by Marie some sixty years ago. It is also held that the primary degeneration of the cells is due to a meningitis about the entering roots causing compression and consequent degeneration of the cells. Others again hold that it is due to the toxins of the Treponema pallidum acting directly or indirectly on the cellular elements of the nerve roots causing them to degenerate. It is possible that the disease is not due to any one of these causes but to a combination of all three.

The changes in the spinal fluid which are always present in the disease I have discussed at length elsewhere and therefore I shall not burden the reader by repeating them here.

Tabes, like its congener, paresis, is more or less a product of the nineteenth century. Previous to that time no mention or description of it can be found in medical literature, although syphilis was more prevalent then than it is now. At the beginning of the

nineteenth century the term tabes dorsalis was applied rather loosely to describe sexual weakness or neurasthenia. But from time to time as the century advanced, investigators, mostly working independently and far apart in time and place, gradually built up the clinical fabric of the disease entity we now know as tabes dorsalis. The sexual weakness which had been considered the whole disease was then assigned to its proper place as a symptom only. The work of Horn, Decker, Romberg, Steinthal and Marie did much to correlate its manifold symptoms and secure its place as a separate and distinct pathologic process. It was Duchenne however, who first fairly described it and studied and discussed it from the modern standpoint. Erb was the first to lay special stress upon its syphilitic etiology, and he was ably seconded by Fournier and Moebius. The latter with much emphasis and speaking with more truth than his contemporaries then realized said, "Without syphilis there is no tabes." These words were uttered more than forty years ago but from that time down almost to the present, opinion has been divided among pathologists, neurologists and syphilologists as to the pathology and etiology of tabes. Not so many years ago the views expressed by eminent men would, in the light of present knowledge, border almost on absurdity. The discovery of the Treponema pallidum and the Wassermann reaction and the examination of the spinal fluid, have altogether altered our former concepts of tabes. It has been established with absolute certainty that it is due to syphilis and naught else. While, as I have already stated, the exact mechanism of its initial pathogenesis is still a matter of conjecture, it is quite certain that it is only a question of time when this too will be thoroughly understood. We know also that tabes can result from congenital syphilis. Not that the disease is hereditary as was formerly erroneously supposed; but certain persons in whom congenital syphilis is present develop the condition by reason of the fact that their nervous system is the *locus minoris resistentiæ*. This explains the presence of tabes in brothers and sisters who are sprung from the same neuropathic stock and who show identical weaknesses in so far as resistance to the infection is concerned.

The vulnerability of the nervous system of certain persons to nervous syphilis has long puzzled clinicians and pathologists. As I have stated elsewhere I am not a believer in the theory of a special strain of treponema having a selective action upon the nervous system. As I have stated, it is my opinion that nervous syphilis is entirely a question of inherent weakness or lack of resisting power which renders the nervous system of some persons more vulnerable to the attack of the disease. Whether this weakness is congenital or arises from extraneous causes not related to syphilis later in life I do not know and, I may add, no one else does. Starkey of Phila-

delphia has advanced the theory that this inherent or constitutional weakness is due to a perversion of the glands of internal secretion, especially the pituitary gland, which so affects the cells of the cord and brain as to render them an easy prey to the infection; or the endocrinic secretions as a whole may be perverted and so affect the sympathetic-autonomic system that the central nervous system is in turn affected thereby. It is possible that this is the reason why syphilis attacks the nervous system of some and not of others. Our present knowledge of the physiology, not to mention the pathology of these glands is so vague and ill-defined that it would be extremely hazardous in view of what the future may bring forth to accept this as the final explanation of the incidence or non-incidence of nervous syphilis in certain persons.

It is a peculiar fact that, as in paresis, in many countries where syphilis is prevalent tabes is comparatively rare. It is quite possible that the same racial factors which go to make paresis more or less prevalent are also operative in tabes.

Period of Infection.—Tabes is essentially a disease of early middle life. The statistics of Grossman, which I believe are correct show that the average age when syphilis is contracted is twenty-four and a half years. The average age when tabes was clinically diagnosed according to Grossman was thirty-nine years. This makes the average pretabetic period fourteen and a half years. Grossman's statistics also show that the length of time between the appearance of the initial lesion and the development of tabes was decidedly shorter the older the patient was at the time of infection; and this leads us to believe that the susceptibility of the nervous system increases with age. This is in accord with the clinical display of syphilis of the aged or rather, in syphilis acquired after the fifth decade of life. The prevalence of nervous lesions in these cases is much greater than when the infection occurs earlier.

Influence of Sex.—Tabes is much more frequent in men than in women. The proportion being approximately ten to one. It is rather more frequent than paresis and its incidence as a tertiary manifestation of syphilis is about $1\frac{1}{2}$ per cent. Why tabes and nervous syphilis generally are more frequent in men than in women is difficult to explain. In fact, at present there is no absolute explanation. There are several theories however; one is that owing to the increased thyroid secretion in women in comparison to men and the consequently greater amount of iodine poured out, the elimination of the toxins of the Treponema pallidum is more greatly favored and therefore involvement of the nervous system is less likely to occur. Another theory which has been put forward by McDonagh is that the naturally greater lymphocytosis in women enables their tissues to resist the infective organism more effectually.

It is certainly true, all things being equal, that syphilis is less severe in women than in men, and this being so, the corollary is equally true that nervous syphilis occurs with much less frequency in women than in men.

Atypical Cases.—Tabes does not always present the typical clinical picture described in text-books. Its symptomatology is often confusing and not always in accord with experience and teaching. The reader should bear this well in mind, otherwise mistakes in diagnosis will occur. There are many cases of tabes which show practically no symptoms except the loss of the pupillary and ankle and knee reflexes. These patients never develop ataxia or any of the other motor or sensory symptoms characteristic of the disease. Not a few of these patients go to their graves oblivious of the fact that they have been for years harboring in their bodies a terrible disease. Again, contrary to its usual mode of attack, the disease may appear suddenly, like a bolt from the blue as it were, and run its course with startling rapidity. Or ataxic symptoms may dominate the picture to the almost complete exclusion of the lightning pains and crises. Or the sensory symptoms may overshadow the motor symptoms and the excruciating pains render life a burden. Or the disease may expend its virulence on the optic nerve alone and cause blindness unaccompanied with ataxia or pain. Or the process may extend upward and implicate the brain —tabo-paresis.

In by far the majority of instances the disease begins insidiously—as insidiously I may say as its congener, paresis. Since it is this beginning stage that holds out the best hope of a cure, and as the symptoms are often—too often I regret to say—diagnosed as something altogether different, it is of paramount importance that they be recognized early, so that early treatment may be given while there is the best chance for effecting a cure. For, as with paresis, in this early stage I believe tabes to be curable. I shall therefore devote some space in this chapter to enumerating these early or prodromal signs of the disease which are almost invariably present before it can be diagnosed with certainty.

In the chapter on paresis I have stated that the time to treat it is before it begins. This seeming paradox holds good with tabes. If the cerebrospinal fluid of all syphilitics in the early stages of the disease was examined, tabes and paresis could be reduced almost to the vanishing point. It is not possible however, to realize this ideal and therefore we must content ourselves with measures less ideal but yet sufficiently satisfactory to yield results that on the whole are almost as good. These are the prompt recognition of the disease while still in its incipiency. It is quite possible to do this.

Premonitory Symptoms.—*Impotence.*—One of the first of the premonitory symptoms of tabes is impotence. Many times it is this loss of sexual power which impels the patient to seek advice. This sexual decadence is never sudden. The patient usually states that he has been noticing a gradual diminishment in his sexual power for a year or more. If, with this history of slowly developing sexual weakness, it is found that the testicles are insensible to pain upon compression it is almost certain that the patient has incipient tabes.

Failing Vision.—Failing vision which cannot be helped by glasses should arouse suspicion and cause an ophthalmoscopic examination to be made for either a beginning papillitis or choked disk, although as Hughling Jackson observed long ago there may be considerable choking of the disk without much impairment of vision. Instead of a gradual general loss of vision scotoma may appear either suddenly or gradually. This limited cutting off of the field of vision may be central, homonymous or heteronymous. I might add in passing however, that choked disk is not always due to tabes. The optic atrophy which causes it may be due to pressure the result of a pachymeningitis in the vicinity of the optic chiasm, or to a neuritis of the optic nerve, or to an embolism of the lenticulate artery or to an aneurysm of the same, or to a thrombus of the central retinal vein or to glaucoma. Not infrequently there may be observed smallness of the pupils—pin-point pupils. Spinal miosis may precede for a long time the Argyll-Robertson pupils, which are characteristic and, when combined with other signs to be mentioned later, are pathognomonic of tabes. In connection with these eye symptoms, however, I desire to call to the reader's attention that these may occur and yet not be syphilitic. The work of Lafon, of Roque and Sergent have shown conclusively that they may be due to intra-abdominal and intrathoracic disease. In particular this applies to the homonymous type. The anisocoria, due to sympathetic or parasympathetic reënforcement, can be distinguished however from that due to syphilis. The non-syphilitic type is most marked in a poor light whereas the syphilitic type is most marked in strong light. Diplopia or double vision is sometimes encountered as a sign of beginning tabes. Also painless development of paralysis of the external muscles of the eye. Meobius was of the opinion that this paralysis of the extrinsic eye muscles was as significant of the disease as the Argyll-Robertson pupils.

Loss of Bone Conductivity.—Loss of bone conductivity as exemplified by Egger's tuning fork test is very suggestive of a beginning tabes. Not infrequently it is the very first objective sign encountered in the disease aside from the findings in the spinal fluid. Sudden deafness is a condition which has been compared by Hermet

to the primary optic atrophy sometimes occurring in tabes. Deafness however may come on gradually. For that reason sudden or gradual deafness from no assignable cause should always arouse a suspicion of beginning tabes.

Lightning Pains.—The so-called lightning pains which are characteristic of the disease especially when it is well advanced, may, in some instances be the first symptoms of which the patient complains. When they occur thus early and before any other signs or symptoms which would otherwise point to the disease they are not infrequently diagnosed as rheumatism, sciatica or neuritis. There are certain peculiarities about these pains however, which are distinct from the conditions named and for which they are so many times mistaken. Chief among these peculiarities is the intensity of the pains and their fleeting, evanescent character. Hence the term "lightning." They are flashes of pain, but flashes so intense and excruciating that it would be impossible to bear them were it not that they come and go like lightning. These pains are not definite in so far as any particular nerve distribution is concerned. When the storm, as it were, has passed—and in the early stage when the process is just beginning, it rarely lasts more than an hour or so—the cutaneous surface where the pains have been is sore and tender to the touch for a day or so after. As pointed out by Strauss purpuric spots may appear where the pains have been. Sometimes instead of purpura the pains are followed by an herpetiform eruption similar to that observed in herpes zoster or shingles.

The pains of muscular rheumatism, no matter how severe, cannot for a moment be compared with the agonizing pains of tabes. The pains of rheumatism, if of the muscles, are diffuse and steady. They may lessen for a time but they never entirely disappear. The pains of tabes come and go with the rapidity of light and then they disappear for days and weeks at a time. If the rheumatism is articular, the joints will be stiff. There is no stiffness of the joints in incipient tabes.

Sciatic pain may be very severe—so severe at times that it may interfere with locomotion, but even so it is not as severe as the lightning pains of tabes. Also, in sciatica the pain follows a definite tract—the course of the sciatic nerve. Sciatic pain is also steady; it does not come and go as do the pains of tabes.

Crises.—The so-called crises of tabes, gastric, laryngeal, rectal or vesical usually do not occur until the process is fairly well advanced. Occasionally however, they are the first symptoms to appear. A sudden attack of indigestion accompanied with pain and vomiting and especially a feeling of weight in the epigastrium; or a sudden attack of diarrhea with marked tenesmus, or a sudden attack of strangury, or a sudden spasm of the glottis lasting for

several hours, should always suggest the possibility of a developing tabes.

Ulcers.—Perforating ulcers on the soles of the feet are usually considered a late sign of the disease but occasionally they are the first. An ulcer on the sole of one or both feet which does not heal should always be considered as possibly trophic and therefore tabetic.

Reflexes.—At this early stage in the development of the disease the reflexes—the patellar, the Achilles tendon and pupillary—are not lost. When they are lost the disease may be said to be fully established and to have passed the prodromal stage.

Diagnosis.—When tabes is established there are certain symptoms which enable a clinical diagnosis to be made with certainty. These are the loss of the pupillary, ankle and knee reflexes, inability to stand with the eyes closed—Romberg's sign—lightning pains, or ataxia. Usually all four of these signs are present but any three of them are sufficient to make a diagnosis.

Sensory Symptoms.—As the disease develops sensory symptoms become more and more manifest. Aside from the lightning pains already mentioned these are tingling and burning sensations in the legs and feet. Areas of analgesia appear. The patient often states that he feels as if he is walking on a quilt or on feathers. These analgesic areas when they occur on the trunk and extremities are usually bilateral. When they occur on the face or head, as in rare instances they do, they are usually unilateral. On the upper extremities the most frequent sites of these analgesic areas are the fingers and the ulnar border of the forearm. A striking feature in some cases is the marked impairment of stereognosis so that the patient is unable to distinguish by the sense of touch the size and shape of objects such as a key or coin. The soles of the feet, the heels and the inner surfaces of the thighs are the usual sites for this analgesia on the lower extremities. On the trunk the regions most frequently affected are over the pectoral muscles and the shoulders and about the umbilicus and the lower part of the abdomen. Quite frequently these areas of analgesia are surrounded by a zone of hyperesthesia. The patient is often unaware of these analgesic surfaces until they are brought to his attention by the examiner pricking him with a pin with no painful result. Less frequent than the areas of analgesia are the areas of hyperesthesia. When these occur they are less symmetrically distributed and they are frequently the sites from which the lightning pains arise.

Anesthetic areas also occur, one of the most frequent of which is the so-called "tabetic cuirass" which is an area about four inches wide encircling the trunk. Occasionally the entire thorax and abdomen may be anesthetic. This anesthetic band is frequently

associated with the "girdle pain;" a painful sense of constriction about the chest.

Incoördination.—Incoördination of the movements of the voluntary muscles—usually those of the lower extremities—or ataxia does not as a rule become manifest until the disease is well advanced. It is in nearly every instance preceded by the sensory symptoms and by the loss of the reflexes. Rarely however, the ataxia may develop before the sensory disturbances. This incoördination develops slowly and for a long time there is no loss in the power of the muscles; except perhaps, the patient notices that he tires more easily than formerly. The patient first notes that he does not walk so well in the dark or in ascending or descending stairs. He also begins to find it difficult to stand without a tendency to sway. This inability to stand without swaying is known as Romberg's sign and is typical of the disease. It can be demonstrated by having the patient stand with his eyes closed when the swaying of the body will be immediately observed.

Gait.—As the ataxia develops a decided change in the patient's manner of walking will be observed. The feet are planted on the ground as it were on a wide base. The eyes are bent downward to watch the faltering steps and to direct the incoördinating muscles as much as possible. As the ataxia increases the slapping gait changes to a stamping. Each foot is raised high and brought to the ground with a stamp. Later, even this grotesque gait becomes impossible and the patient cannot even stand without support. The ataxis stage has passed and he has now reached the final or paralytic stage in which he ekes out the remainder of his days in bed or wheeled about in a chair.

Ataxia of the upper extremities is less frequent than of the lower. Not infrequently it is entirely absent. In rare instances it may occur before ataxia of the lower extremities.

Condition of the Muscles.—The musculature, especially of the muscles of locomotion always show more or less hypotonus. This is exemplified by the fact that in tabes when the patient is placed on his back he can raise his leg to an angle of ninety degrees with the plane of the body, whereas in health he cannot raise it to an angle of more than forty degrees. The reason for this is that the tonicity of the semimembranosus and semitendinosus is entirely lost so that they no longer resist. This hypotonicity is also shown by the patient being able to flex the knees to such an extent that the heel can touch the buttocks in voluntary motion. This hypotonus of the muscles of the legs and of the ligaments of the knee joints gives the legs a backward bowing which is very characteristic. True atrophy of the muscles is not often seen except in connection with the general wasting coincident to the disease. When atrophy

occurs the muscles of the feet and legs are most frequently affected. Occasionally there is atrophy of the muscles of the forearm and hand.

In tabes there is sometimes to be noted coarse choreic movements of the legs or arms not unlike Huntington's chorea. Paralyses not infrequently occur in the course of the disease—monoplegia, hemiplegia, paraplegia, paralysis of the tongue or of the laryngeal muscles, various forms of facial paralysis—especially as before noted, ptosis.

Visual Defects.—Besides the Argyll-Robertson pupils which are present in from 50 to 70 per cent of all cases, other pupillary anomalies are inequality and irregularity. In a certain number of cases, estimated at approximately 10 per cent the disease seems to spend its virulence upon the optic nerve exclusively. In these cases blindness supervenes but ataxia and the lightning pains are absent.

Auditory Defects.—According to Murpurgo auditory defects are present in 80 per cent of all cases of tabes. These include besides the sudden or gradual loss of hearing already mentioned, various recurring or continuous sounds such as the ringing of bells, rushing water and muscial sounds.

Trophic Disturbances.—Trophic disturbances are of frequent occurrence during the course of the disease. These consist of hyperidrosis or anidrosis which may be general or confined to some particular part, alopecia areata, perforating ulcers on the soles of the feet, herpetiform eruptions. Also included are loss of the teeth due to involvement of the trifacial nerve and to pyorrhea to which tabetics are particularly prone. For the same reason owing to the decalcification and rarefication of the bones, fractures, especially of the long bones, are apt to occur from very slight cause.

Charcot's Joint.—Perhaps the most frequent, and certainly the best known of the trophic disturbances of tabes is the arthropathy known as Charcot's joint, so named from the great French neurologist who was the first to describe it and assign tabes as its cause. Some pathologists are inclined to believe that this particular arthropathy is not due to trophic disturbance but that it is a distinct syphilitic disease of the joint. Be that as it may, this particular arthropathy is frequently present in tabes. The capsule of the joint—usually the knee, although sometimes it may be the elbow—becomes filled with fluid causing the joint to assume a globular form. The synovial membrane is thickened and there is destruction of the cartilages and the articular surfaces of the bones—in other words, complete disintegration of the joint. Should it become infected with pyogenic organisms, suppuration occurs, which because of the already debilitated state of the patient is of grave import. The condition gives rise to great deformity of the joint—the so-called "flail joint," which renders the leg useless.

Crises.—I have already mentioned the crises of various kinds which are sometimes present during the course of the disease. In not a few instances however they are entirely wanting. When occurring early in the disease they are not infrequently wrongly diagnosed, which, when we consider their somewhat vague and indeterminate character, is not surprising. The most frequent and therefore the best known of these somatic explosions is that occurring in the gastro-intestinal tract. Without any previous warning and in the absence of any dietary indiscretion the patient is seized with sudden and violent pains in the stomach and intestines accompanied with vomiting and diarrhea and more or less prostration. The attack lasts for several hours and then ceases as suddenly as it began. In some instances there is no abdominal pain or vomiting, the disturbance being confined to the lower bowel. There is diarrhea and tenesmus which may be so intense that the thin and watery stools that are passed may be tinged with blood.

Next in frequency are the laryngeal crises which are also sudden in appearance. They are due to spasm of the laryngeal muscles. There is dyspnea and noisy inspiration and sometimes cough and pain. In rare instances there are nasal crises in which the patient is seized with an uncontrollable sneezing fit.

Bladder Disturbances.—In view of the fact that the lumbar region of the cord is usually the primary seat of the disease, involvement of the bladder is frequently observed as an early as well as a late symptom of tabes. In the early stage of the disease there is in quite a number of cases a seeming paralysis and insensibility of the bladder. The patient urinates slowly and is unable to expel all of the urine contained in the bladder. This residual urine accumulates and it is surprising how much urine may be contained in the bladder without the patient being aware of it. In time the bladder may become infected because of the constant presence of this residual urine and cystitis and pyelonephritis may develop. In this event the patient will have a low continuous fever due to absorption of toxic products in the bladder and kidneys. In the later stages of the disease there may occur vesical crises in which there is frequent micturition with more or less vesical tenesmus sometimes followed by acute retention.

Cause of Death.—Tabes, *per se,* rarely causes death; the patient usually succumbs to some intercurrent affection during the course of the disease due to his weakened and debilitated state. Chronic myocarditis is a frequent cause of death in tabes as a very large number of tabetics are affected with cardiac valvular lesions. It has been said that tabetics frequently die of phthisis pulmonalis; this has not been my experience however. Should the patient escape

death from cardiac disease, pneumonia, or chronic nephritis, he may live for many years and finally die a bed-ridden paralytic, of asthenia.

Pseudotabes.—The pseudotabes of chronic alcoholism or arsenical poisoning or diabetes offer no clinical difficulties in diagnosis. The steppage gait of these conditions is quite unlike the ataxic gait of tabes. In these forms there is a paralysis of the feet and the legs are lifted high in order that the toes may clear the ground. The lightning pains and crises are absent, and the pupillary reflexes are normal which in tabes is exceedingly rare. Erb's spastic paralysis and multiple sclerosis are sometimes confused with tabes, but a careful survey of their symptoms as compared with those of tabes should at once make plain the diagnosis. Most important in establishing the diagnosis is the examination of the spinal fluid from which there is no appeal.

Treatment.—The treatment of tabes is the treatment of nervous syphilis generally. That is, it consists in intensive arsphenamine and mercurial treatment—intraspinally and intravenously. The indications for these are largely governed not only by the clinical symptoms but most especially by the cytology of the spinal fluid. These indications both as to treatment and prognosis are discussed in the chapter on the Treatment of Syphilis, particularly that part which deals with the special technic in the treatment of the nervous forms of the disease. The reëducation of the muscles, whereby the patient is supposed to learn to walk again as exemplified by the methods of Fraenkel, Maloney and Collins, I do not believe are of much benefit. If the process can be arrested and the patient's general health improved his gait will naturally improve provided there has not been too much destruction of nerve tissue. If there has been much destruction of nerve tissue, it is useless, in my opinion, to try to teach him to do what, if we analyze his condition fairly and dispassionately, he cannot do, because the controlling mechanism of the muscles of locomotion is injured beyond repair. The education of uninjured tracts, upon which this theory rests, is in my opinion a fallacy.

CHAPTER XXXIII.

SYPHILITIC PSYCHOSES OTHER THAN PARESIS.

The role of syphilis as a causative factor in mental affections other than paresis has been suspected only since 1879 when Fournier expressed the following opinion: "While syphilitic insanity has not yet a distinct place in nosology, nevertheless I think that syphilis is apt to create cerebral disorders which may be considered as indisputable forms of insanity." Since then the relationship of syphilis to psychoses as cause and effect has been studied by but few observers, although the importance of the subject cannot be overestimated.

Mental Disturbances of Syphilis.—In 1917, Gordon of Philadelphia published in the *Journal of the American Medical Association* the results of his observations on 23 cases of syphilitic psychoses with the hope of elucidating some features of this problem. His series was divided into two groups. In the first were 5 cases occurring in the secondary stage; the second group consisted of 18 cases in the tertiary stage of the disease. His analysis tends to show that while the mental disturbances during the secondary stage could be considered with a great degree of certainty as being directly due to the syphilitic toxemia, the same degree of certainty could not be entertained in regard to the relationship of the psychoses developing during the tertiary period. In the former the mental disturbances were in every instance analogous to those which we observe in toxic infectious states of any origin. The confusional, hallucinatory and delirious states paralleled the secondary manifestations accompanied with fever. When the latter disappeared the mental symptoms commenced to improve. It was also noted that antisyphilitic treatment exercised a manifest and favorable effect upon the mental phenomena. In the other group various psychoses had developed many years after the initial infection. These cases presented the typical pictures of classical psychoses of various types, such as Korsakoff's syndrome, manic depressive insanity and dementia paranoides. Gordon could form no definite opinion as to the direct relationship between these psychoses and the infection which had occurred many years previously. The reason for this is quite obvious. It is most difficult to differentiate between symptoms due to syphilis and symptoms arising from other diseases which the

patient may have and which have no connection whatsoever with the luetic infection. The fact that a patient has had syphilis is no reason why he should be immune to other diseases and it is folly in many instances to ascribe all of his subsequent ailments to the luetic infection. A syphilitic is just as susceptible to a psychosis or a neurosis after having had syphilis as he was before—perhaps more so, especially if his nervous system is his point of greatest susceptibility. But again, it has been observed that psychoses occurring in syphilitic individuals present certain peculiarities as it were which can be justly attributed to the influence of the syphilitic disease.

Characteristic Mental Symptoms.—The various mental symptom-groups which have been described as characteristic of syphilis were long ago described by Wille, but it is due to the more recently recognized pathologic potentiality of syphilis on the central nervous system that the term syphilitic psychosis has come to occupy a more prominent position. After a long abeyance, syphilis as a factor in mental disturbances has again been discovered as it were. But it must be said, however, that as yet no definite or fixed limitations have enclosed the symptom group thus rubricated. It cannot be gainsaid that in this connection the greatest diversity of opinion obtains, as is natural when opinions are based on unsatisfactory observations. Some observers delineate disease pictures as absolutely characteristic of cerebral lues which are denied with equal decisiveness by others. But as I have already stated without restriction to any particular characteristic type of psychic disturbance, the term syphilitic psychosis appears to be a definite reality.

Among the earlier attempts to describe a characteristic abnormal symptom-complex pathognomic, as it were, of cerebral syphilis certain depressive and anxiety states connoting syphilophobia or a more generalized hypochondria have been given. These were looked upon as the prodromal phase of the syphilitic psychoses; the concluding picture being a progressive deterioration.

I do not deny that such a condition may exist but I am convinced from extensive observation that not all cases—in fact comparatively few—ever go on to the extent mentioned above.

Syphilophobia and Syphilomania.—Every syphilologist and every practitioner of general medicine comes in contact with these individuals It is a condition as old as syphilis itself. When a patient knows he has syphilis he is often in a state of fear—not always, of course, but often enough. With some individuals this state of fear is more intense than in others. It is these individuals who become true syphilophobes. The patient's malady presents a true *idée fixé*, an obsession or even a systematized delusion, and he can no longer be treated like a man who is simply fearful or anxious

in the ordinary way. Naturally a man like this, even if his syphilis has never troubled him, can become insane on the subject. In 1869 Diday made the distinction between syphilophobia in the non-syphilitic which he termed syphilomania and syphilophobia or the same condition when it existed in a syphilitic. Syphilomania when fully developed is a real obsession on the part of a non-syphilitic individual that he has syphilis. In many instances these patients are practically incurable; they can never be convinced otherwise and their obsession continues as long as they live. In not a few instances these cases arise from the visiting of quacks who for mercenary reasons create the impression in the patient's mind. However this may be, these individuals are almost always neuropaths and degenerates or are already mentally alienated. The false impression created simply brings the mental state to a crisis and gives it a direction as it were. These patients pay no attention to the natural phenomena of the disease. Every little pimple, every little pain or ache, real or imaginary, they attribute to the disease, which to them is a sort of personification of evil. Syphilophobia occurs only in the syphilitic. It may be only temporary, and under the wise counsel and encouragement of his physician it soon passes away. It may however be incurable. The fact that the patient has contracted the disease may inflict such a deep mental wound as it were that he never recovers. These patients are natural neuropaths, and following along the path of least resistance it not infrequently happens that they finally terminate in paresis or some other form of mental deterioration.

While recognizing this hypochondriacal introduction as a possible beginning of mental disorder due to lues, it must not be forgotten that it does not always lead to this; it may exist in another form than syphilophobia. It must also be remembered that the ultimate dementia may be preceded by an excitement, a delirium or a mania, in which the premonitory hypochrondriacal state was missing.

These abnormal mental states presenting themselves early in the disease are considered by some, and with reason many times, I think, as initial symptoms—stages in a developing psychosis. For that reason an attempt has been made to segregate them as distinct types of mental disorder characteristic of syphilis involving the brain. Because of this the terms syphilitic melancholia, hypochondria, paranoia, amentia and dementia are used. The last of these—dementia—has been found to occur so frequently in brain syphilis that it has become to be regarded as characteristic of all mental maladies associated with syphilitic disease of the brain.

In reality, by that I mean from the strictly clinical standpoint, the classification of the different manifestations of brain syphilis is not a matter of prime importance. It is much more important

to be able to recognize that a mental disorder when encountered is due to syphilis and nothing else. But it is here where we come in contact with the very great difficulty at times of distinguishing between coincidence and cause. The question resolves itself into what differential diagnostic data we have at our command. Mental disorders arising during the devolutional epoch, those dependent upon arteriosclerosis and other senile changes are the cause of many difficulties in differentiation. It is also to be noted that syphilis of the brain may occur in an individual in combination with or superimposed upon some other mental disease, such as for example, dementia præcox. There are many records of such cases in which the ultimate solution of the problem rests in the hands of the pathologist. There are, however, certain criteria which greatly aid in the recognition of morbid mental states resting upon a syphilitic basis.

We know that mental disorders associated with acute and subacute meningo-encephalitic forms of cerebral syphilis are much more distinctive of their luetic origin than are the more chronic types. The latter are more frequently mistaken for arteriosclerotic psychoses or paresis. The reason for this is because many of the simpler forms of dementia occur as expressions of chronic meningo-encephalitis. When we consider the wide variety of anatomical lesions which may be produced by syphilis in the central nervous system—inflammations of the membranes, especially at the base, gummata, and arteritis, it is to be expected that from such anatomic substrata very many clinical manifestations might arise. Krause is of the opinion that with the basal type of brain syphilis the mental symptoms are of secondary importance and occur at a comparatively late period in the course of the disease. With the meningo-encephalitic forms, involving primarily as they do the convexity, the psychical symptoms appear much earlier. It is in these forms that we have confusion, sopor, delirium. The arterial forms are associated with cephalalgia, syncope and periods of stupidity. Mentally there is less activity or less irritability.

Cerebral Syphilis.—Theoretically cerebral syphilis is to be sharply distinguished from paresis, but clinically this differentiation is often extremely difficult. Cerebral syphilis, pathologically speaking, may be said to be more on the surface, as contrasted with the parenchymatous changes of paresis. There are three types which may be combined to a certain degree: The gummatous, which is the rarest; the meningeal; and the vascular, which consists of a girdling obliterative endarteritis.

From the very nature of cerebral syphilis it is plainly evident that the symptoms are most apt to be of a focal variety, such as paralyses of varying types and degrees. As pointed out by Adolph

Meyer, "The mental symptoms are those of all organic disorders—memory and retention defects, states of confusion and hallucinations—but with the relatively little unaccountable and fundamental change of character and dilapidation of the personality."

Symptoms of Cerebral Syphilis.—It has been stated that the Argyll-Robertson pupil is rarely present in cerebral syphilis. But with this I cannot agree. The general symptoms of cerebral syphilis as distinguished from those of paresis are headache, dizziness, insomnia, lack of concentration, fatigue, and sometimes focal vomiting, cranial nerve palsies. Speech and writing are unimpaired and there is absence of facial tremor. It also occurs earlier than is usual with paresis. Further, and this is most important, it offers a much better prognosis than paresis. It is possible at times to cure cerebral syphilis, but paresis is incurable.

Syphilis as a Cause of Mental Disorders.—In considering the possibility of syphilis in causing mental disorders, Barnes emphasizes the following: (1) There is no mental symptom-complex characteristic of syphilitic disease of the nervous system. (With this I fully agree.) (2) Many types of psychoses may be simulated by mental disorders caused by syphilis. (3) Cerebral syphilis may develop in a brain already infected with mental disorder and may occur in conjunction with other organic diseases of the brain. (4) Paralysis, paresis, and convulsive episodes may be absent when the mental disturbance is caused by syphilis. (With this I also agree.) (5) The differential diagnosis is frequently difficult and often impossible.

There are, as Barnes states, many elements of uncertainty in making a diagnosis of mental disorders due to syphilis alone. Innumerable statements can be found throughout the literature which cast grave doubt on the claims made from time to time by various observers that any given psychopathic condition is due to syphilis and nothing else—is pathognomonic as it were. If an attempt is made to lay down certain hard and fast rules upon the subject, a number of questions arise which must be taken into consideration. One is the question of syphilis. This is comparatively easy to answer. The serological and cytological tests will answer that. Another question is the very frequent existence of causes other than syphilis which contribute wholly or in part in creating the morbid mental state. Among these we include alcoholism, senility, renal and cardiac diseases and tumors of non-specific origin. If it were possible to first prove the existence of a syphilitic lesion and then to exclude alcoholism and non-specific vascular changes, there is no doubt but that much that has been written would be cast aside. It seems to me that the mode of reasoning by many observers is something like this: "Here is a case of organic

brain disease. The Treponema pallidum has a predilection for the nervous system and is the cause of most organic brain disease. It is therefore antecedently and consequently probable that the patient has had syphilis and his syphilis is the cause of his cerebral dyscrasia." Of course this is not sound reasoning; nevertheless it is offered up as such, usually with much scientific side-dressing.

An instance of this is to be found in the psychopathic state caused by syphilitic new growth of the brain. But is it possible to distinguish between the psychosis produced by a specific and a non-specific tumor? We must also consider syphilitic hypochondriasis, syphilophobia and insanity occurring at the very onset of the disease. In all of these conditions, lowered nutrition of the brain, which may be entirely functional, is capable of accounting for them and it is not really necessary to consider syphilis in explaining them.

Mott considers "stress" to be the important proximate factor in the development of brain syphilis in an individual affected with the disease. In this regard I am in accord with him. But "stress" is, however, perhaps equally the proximate cause in psychoses where syphilis is not concerned.

In manic-depressive conditions we have to deal absolutely with an insanity that is hereditary. Nearly if not all observers agree that they have never seen a case of manic-depressive insanity in which a distinct family history could not be elicited. There is no reason why an individual with such a heredity should be exempt from contracting syphilis. A psychopathic individual can have syphilis the same as any one else. Such an individual having syphilis and showing manifestations of manic-depressive or some other psychopathic state will also show in his blood and spinal fluid the reactions of a syphilitic infection and we will get improvement in so far as the syphilis is concerned when antisyphilitic treatment is administered. We can also get improvement of the mental symptoms because ordinarily these patients tend to recover. The point I wish to elucidate is that the two conditions may exist side by side as it were and yet be entirely separate and distinct as disease entities.

Aside from the structural changes which the Treponema pallidum may produce in the central nervous system there is also the possibility of a psychogenic mental disturbance which may develop in the individual who is confronted with the new and distressing problems which arise in one who has acquired syphilis. It is not uncommon, as every syphilologist knows, for functional mental disturbances to occur in the early stages of syphilis, the only explanation for which is the fear consequent upon infection. Now it is a well-known fact that manic-depressive psychoses often have their

beginning in a disturbance of the normal moods brought about by some troublesome situation. This accounts therefore for many of the psychoses which appear in this stage of the disease.

Neurasthenia.—During the secondary stage of syphilis neurasthenia is a not infrequent manifestation of the syphilitic toxicosis. It is undoubtedly favored if not actually induced by the reaction occurring in the tissues to the syphilitic poison. Another factor, not always recognized, because many physicians lack that quality which makes for real keenness of intellect—imagination—is the psychical trauma, the effect on the mind of a sensitive individual whose moral sense has received a profound shock by reason of the acquirement of what he knows to be a loathsome and probably incurable disease. This knowledge naturally renders him morbidly apprehensive not only of the danger to himself but to his wife and offspring. His mind, therefore, continually dwells upon the subject with ofttimes disastrous results. Powers and Murphy are of the opinion that the terrible "ripper" crimes of three decades ago were committed by some homicidal paranoiac who had acquired syphilis and who was impelled by the delusion that he had a mission to rid the world of prostitutes who disseminated the disease.

The symptoms of neurasthenia occurring in the secondary stage of syphilis do not differ from those shown when acquired from some other cause. If the condition is dependent upon the anemia and toxemia of the luetic disease antisyphilitic remedies will bring about a cure, coupled as they should be by wise suggestive therapeutics on the part of the physician.

In so far as syphilitic neurasthenia is concerned, I am in accord with Fournier who states that those cases in which the neurasthenia comes on early in the disease usually get well after a period of a few months. The neurasthenia which appears in the tertiary stage of the disease and which is apparently independent of specific manifestations is much more persistent and nearly always results in a lasting disturbance of the mental equilibrium. As a rule these cases are not benefited by antisyphilitic treatment.

Epilepsy.—A disease in which there is often a syphilitic basis is epilepsy. This does not hold in those cases appearing in childhood or adolescence but in those which appear after thirty-five years of age. Unless trauma can be excluded I would say that such cases are often syphilitic unless we consider the possibility of a non-specific tumor of the brain.

Dementia.—In basic syphilitic meningitis a semi-somnolent, semi-conscious or a semi-comatose condition in which the mental functions are more or less obtunded rather than obliterated is usually present. As a rule the patient can nearly always be aroused sufficient to become aware of his surroundings. Thus the patient

may be able to answer the questions put to him in a slow, drawling, sleepy manner. He may even perform complex acts in response to requests or commands, yet be unable to respond to the calls of nature and so passes urine and feces in the bed or in his clothes. Occasionally the patient may shamelessly masturbate. The mind may again become clear and control of the power of urination and defecation return but not infrequently this control over the sphincters is not regained. In such cases permanent dementia usually sets in. The dementia of syphilitic brain disease is characterized by being partial and recurrent. It does not alter the character and personality of the individual to the same extent as the dementia of general paresis. These patients preserve to a remarkable degree their autocritical faculties and they are usually conscious—sometimes acutely so—of their intellectual deficiencies and they are usually by no means indifferent to their bodily condition.

A feature of syphilitic insanity as distinguished from paresis is that such insanity presents possibilities of cure which paresis does not. This, notwithstanding the intraspinous and intraventricular methods of medication now in use.

Paresis.—It has not been so long ago that syphilis was only suspected as a cause of that most terrible of mental diseases—paresis. Those who insisted upon syphilis as the only cause were often laughed out of court by the medical wiseacres of the day. But now we know that these wise clinicians were far in advance of their generation, and we honor them. Slowly the evidence came to light—a little here, a little there, until finally the structure was complete. First it was that only 80 per cent of paretics were syphilitic; then the percentage climbed to 90 per cent. Then someone made the statement that 99 per cent were syphilitic and the other 1 per cent were suspicious. Then came the discovery of the Treponema pallidum and then Noguchi's finding of the organism in the brains of paretics. The evidence was complete and the doubters were silenced once and for all. The history of the development of the etiology of general paresis is especially interesting from the viewpoint that yet exists in regard to the etiology of the so-called functional neuroses and psychoses. Everything is blamed, from heredity (a vague abstraction) to environmental conditions, masturbation, and what not. That these are solemnly affirmed to be the cause of a variety of so-called functional neuroses and mental disturbances is absurd.

Syphilis and Insanity.—It is highly significant that investigators are obtaining high percentages of positive Wassermanns in institutions for feebleminded and the insane. Nor does a negative Wassermann absolutely rule out syphilis, especially if other clinical evidences are present. Decidedly suggestive is the fact that out

of 151 adult neurasthenics, 38 or over 25 per cent admitted lues, and that 75 or over 49 per cent gave evidence of hereditary lues either in stigmata present in the individual or in the family history. These are facts that cannot be denied and they show beyond all doubt what an important factor syphilis really is in the causation of both feeblemindedness and insanity.

Among the diseases which affect the brain in the earlier years of life and which may lead to dementia and other psychoses, syphilis plays a most important role. It is a knowledge of this fact that has gradually opened the way to separate certain mentally defective children whose defectiveness is based on heredity from the great mass of other forms of feeblemindedness. Investigations into the syphilitic antecedents of feebleminded children have been made from various angles. English and American statistics for some reason show the lowest figures. Whether this is due to a lower incidence of the disease amongst the Anglo-Saxon as compared with other races I do not know. In 1000 idiots Shuttleworth found only 4 cases of positive and 10 cases of probable syphilis. These figures seemed even to him to be too low. Down in his idiot material found only 1½ per cent of syphilis. On the other hand, the German, Wildermuth, estimates the frequency of hereditary syphilis in idiots at 11.8 per cent. Binswanger in an institution exclusively for imbeciles of the better social class found 9.5 per cent certainly and 12.2 per cent probably syphilitic. König found in simple idiocy, not complicated by any motor disturbances, hereditary syphilis positively present in 6.5 per cent and strongly probable in 4.2 per cent, making a total of 10.7 per cent. The Frenchman, Bourneville, believed syphilis to be an extremely rare cause of idiocy. The statistics of Huebner are in striking contrast, however, to Bourneville. In a census of 25,000 treated in the Charité, there were 230 cases of idiocy. Of these in 87 etiological information was obtainable. Syphilis was present in the parents of 23 per cent, nervous hereditary taint in 20.7 per cent; symptoms of fever in 16 per cent; alcoholism in 13 per cent; the remaining were due to other causes. According to Heubner's statistics syphilis leads to an etiological factor in idiocy.

Plaut does not believe it probable that syphilis produces a severe grade of feeblemindedness. He believes it improbable because we must here introduce as a cause, syphilitic brain disease developing in utero; and while it is well known that syphilitic disease of the embryo often takes place, it almost inevitably results in death of the fetus. Therefore syphilis cannot be regarded as a factor in causing congenital idiocy. Idiocy of a marked grade however may is present in syphilitic children due to syphilitic brain disease occurring in infancy. The reader can readily understand the distinction. In

the vast majority of instances the condition is inaugurated in this manner—the development of infantile syphilitic brain disease. In some instances the onset is insidious and chronic from the onset and not fulminant as is usually the case.

Feeblemindedness.—The type of the hereditary syphilitic child without any tangible evidences of brain involvement has been graphically described by Fournier. These children are backward mentally and physically. They are unintelligent, simple, silly, limited. They develop slowly and with difficulty both mentally and physicially. They are late in erupting their permanent teeth and remain small, anemic and stunted. Also, they talk late, learn to read and write with difficulty, their vocabulary is small, their memory faulty. At the age of ten or twelve years their pleasures and plays are still those of much younger children. When they grow up they are poor scholars, weakly endowed, do not advance and are always behind their companions. Thus they stay, scarcely developing further, always inferior, and with limited mental capacity. The picture drawn by Fournier is absolutely true to life as every syphilologist knows. But, as Fournier strongly emphasizes, such a child "is not an imbecile or an idiot." These children represent in mildest terms the purely mental form of hereditary syphilis. Yet from the relatively mild disturbance represented by these cases severe weakmindedness may develop either slowly or with startling suddenness. Fournier's opinion is further confirmed by Ziehen who reports that after a careful statistical study in mild congenital weakmindedness he found hereditary lues probable in 17 per cent and absolutely certain in 10 per cent of cases.

Moron.—Other forms of congenital syphilitic weakmindedness in which the intellectual is much less marked than are disturbances in the moral and emotional qualities—the moron type or the criminal type, have been observed. In this connection Pieper describes two hereditary syphilitic children who apparently belonged in this class. One was a boy who from childhood showed an excitable, choleric, destructive nature. Since his eleventh month he had convulsions but with no paralysis. The other, also a boy, whose father had syphilis and was psychopathic, as an infant showed definite signs of hereditary syphilis. Between his first and third years he had convulsions. When he grew up he went to school but was a very indifferent scholar. He committed many foolish acts, among which was an attempt at suicide with oxalic acid.

Hereditary Syphilis as an Etiological Factor.—Neurasthenia on a basis of hereditary syphilis is described by Kowalewsky. Kraemer also is inclined to favor hereditary syphilis as a factor in causing the various neuroses in children. The consensus of opinion amongst

all observers is that there is a psychological inferiority in syphilitic children in which the involvement of the intellect is not the only feature.

The question will arise, how can we recognize in a weakminded child that the mental disturbance is due to hereditary syphilis? The answer to this question is most difficult. The psychical picture does not show us anything that cannot be due to other causes. There is little of differential diagnostic value, or at least we are not yet in a position to recognize such peculiarities if they exist. There is one symptom, and I may say only one, that is of value, and that is the behavior of the pupillary reaction. If this shows disturbance in that it is immobile to light or unequal and irregular and there is facial tremor and loss of the knee jerk, we may assume with considerable probability that a syphilitic process is the cause of the disease picture. Absence of these signs, however, does not by any means preclude syphilis. This fact must be borne well in mind. Therefore, since the essential psychical and neurological disturbances present do not always enable us to form a judgment, we must rely, so far as syphilis is concerned, upon the history, the presence of stigmata and the serological and cytological reactions.

The history directed to the proving of syphilis will include the parents, the brothers and sisters if any and the child itself. The course of the pregnancies of the mother will furnish valuable information—abortions—dead children—full term syphilitic child—syphilis-free child. Many times the anamnesis is so strikingly characteristic that it is not necessary to go further. Again it may be so vague and contradictory as to be of no value whatsoever. But there is one outstanding fact that is always to be considered. We can, in most instances, without any further doubt conclude that a weakminded child is such on the basis of hereditary syphilis when we can prove absolutely that the father is syphilitic. If the child has never shown any of the signs of syphilis; if in the series of births of which it is one, there have been no abortions, miscarriages or dead-born children, nevertheless we can always assume the possibility of a relationship between the mental dyscrasia and inherited luetic disease.

There is further difficulty in assuming syphilis in cases of this kind because syphilitic brain disease can run its course without showing any of the external or grosser manifestations of syphilis. It cannot be denied that in many instances these are present with such clearness that they constitute a positive diagnosis. But difficulties also arise here. Take for instance the classical Hutchinson's triad—notched teeth, interstitial keratitis and deafness. None of these are to be found in infants. Again, there are some

who do not consider that these signs are always pathognomonic of inherited syphilis. We have, therefore, to look elsewhere for some objective sign that cannot be impugned. This fortunately we have in the serological and cytological reactions which occur both in inherited as well as in acquired syphilis. It does not follow that in every case of feeblemindedness that shows a positive Wassermann that the condition is due to syphilis *per se*, but if such is the case the possibility of the syphilitic factor in the etiology of the condition must receive grave consideration.

In concluding this chapter the question to be decided is: Can syphilis *per se* produce mental disorders? Are we ready to accept Ziehen's statement, "Syphilis is one of the most important factors in psychopathology?"

The literature on the subject is meager. As yet it is difficult to establish an absolute casual relationship to all forms of psychoses. But it seems probable—in my opinion more than probable, so much so that it is in very many instances an absolute certainty—that syphilis may cause any type of mental disturbance. Those patients who are already afflicted, or inclined by reason of inherent weakness, are in my opinion rendered worse by syphilis.

I would also say that syphilis is, in my opinion, the most important of all factors in causing insanity.

Aside from the clinical facts herein detailed, the serological and cytological signs are of supreme importance. In determining a given case, recourse must be had to these before a positive diagnosis can be made. I refer the reader to the chapter on Serology for further information.

CHAPTER XXXIV.

SYPHILIS AND TUBERCULOSIS.

Tuberculosis ranks with syphilis as being one of the most widespread of diseases. From the tropics to the regions of perpetual ice both are found, and it is not strange therefore that the two should meet in the same individual and each inflict its separate woes upon him. Such often happens, and it is my purpose in this chapter to discuss their influence as separate disease entities upon the bodily organism. The presence of the two diseases in the same patient frequently confronts the physician—especially the general practitioner—who as a rule is the first to see them, and it is to him many times one of the most important problems of syphilis and—I may say—of tuberculosis as well.

Tuberculosis a Cause of Death in Syphilis.—Considerable data have been published concerning terminal tuberculosis in syphilis. The mortality percentages show much variation, but it has been pronounced the most common single cause of death in syphilis. I am not in accord with this, but I am willing to admit that tuberculosis undoubtedly is an important factor in causing the death of all syphilitics under thirty years of age. These are those who in most instances have a predisposition to the disease and the cachexia which develops in the secondary stage of the disease renders them an easy prey to the secondary infection of the tubercle bacillus.

Relation of Tuberculosis to Syphilis.—It is not possible to determine how the bacilli enter the body, but, in this early stage of syphilis, angina is an important manifestation, and it is possible that these lesions of larynx and pharynx are the portals which afford entry for the tubercle bacilli. In these patients the syphilis and the tuberculosis both run a severe course. There are exceptions to this, however, which are as follows: If the tuberculosis is still in the incipient stage, while the tuberculous foci are still localized and the general health has not suffered, the syphilis will not necessarily be grave, although it is still apt to be more severe than if it occurred in an otherwise healthy individual. If the tuberculosis is advanced when the syphilitic infection is incurred the syphilis will be severe. But between these extremes there are many gradations and it is not possible, therefore, to lay down any hard and fast rules. If the syphilis is promptly treated and the tuberculosis is of the

fibrotic type it is quite possible that the syphilitic infection will have comparatively little influence upon the tuberculous disease. Gummata of the joints or of the bones are frequently complicated with tubercle and the same is true of lupus, which may be complicated with a syphilitic lesion. In such cases the prognosis of both diseases is rendered more grave and they both more or less interact in a deleterious way upon each other. In these cases the destruction caused by both infecting agents is always greater than if the attack were confined to one alone. In such cases the syphilis should be attacked first because it is easier to clear up than the tuberculous disease. After the syphilitic infection is disposed of, the tuberculous disease should be treated after the method suited for the individual case. These cases, I may add in passing, are not hybrids as some suppose. Each is separate and distinct although the appearance may be confusing. They simply represent two distinct infections attacking the same part at the same time.

It has been said by some that tuberculosis predisposes to syphilis. The reasons given for this are that the patient with tuberculosis leads a more active sexual life than those free from the taint; also, that the debilitated state of the health occurring in the course of the disease renders such patients more susceptible to infection. The last statement may be true although any other debilitating disease would have the same effect. That the tuberculous are more active sexually many eminent authorities deny. It is a question that I will not pass upon, as I am not a phthisiologist. Personally I am inclined to believe that the tuberculous are no more liable to contract syphilis from this cause than from any other. In the advanced stages of the disease, I think even less so, because of the quiet and more or less secluded life they are obliged to lead. There is infinitely more evidence that syphilis plays an important role as a predisposing factor in the development of tuberculosis. Syphilologists and phthisiologists will both agree to this. Syphilis furnishes the soil upon which tubercle can flourish. Fournier has stated that he has often seen young syphilitics go into rapid consumption. He does not hesitate to states further that the syphilitic infection is wholly responsible for the subsequent tuberculous disease. As Landouzy said long ago, "syphilis often makes the bed of tubercle." With this I am in full accord. The eminent French clinician, Sergent, has expressed the opinion that syphilis can create unassisted by any other cause a terrain for the propagation of tubercle. This would include in my opinion the hereditary syphilitic rather more than the one who acquired the disease later in life. It is easy to understand that the debilitating effect of hereditary syphilis can do this by the terrible handicap which it places upon the individual's resistance from birth. When late syphilis leads to tuberculosis

there are not infrequently other factors, such as alcoholism and bad hygienic surroundings, which also help to debilitate a system already depressed by a disease which vitiates every tissue of the body.

When syphilis in the secondary stage leads to the development of tuberculosis it is undoubtedly due to the profound anemia which it causes. It is then that the tuberculosis, perhaps latent or perhaps acquired, because of the depressed condition of the bodily forces, explodes, as it were, just as it might do under some other analogous condition. It is therefore absolutely necessary where tuberculosis is suspected, or where it is probable that it may develop, that the patient should be placed under the best hygienic conditions and the body further fortified by cod-liver oil, super-diet in the way of milk and eggs, milk, sugar, fresh air and rest. In fact the treatment should be that of syphilis plus that of tuberculosis. This applies, I may say, not only to those who already have the tuberculous disease but to those who are threatened with it as well. In other words, "an ounce of prevention is worth a pound of cure."

It has been stated that tabetics show a decided tendency to develop tuberculosis. Personally I have not observed this and I am inclined to doubt it, as tabes usually develops at a much later age than tuberculosis.

Prognosis.—When we regard syphilis as something added to tuberculosis, or tuberculosis added to syphilis, the question at once arises as to how the prognosis is influenced. The question is not difficult to answer: both diseases associated in the same individual always exert a deleterious influence upon each other and consequently upon the host of the two infections. But there are undoubtedly seeming exceptions to this. A patient with mild tuberculous disease who contracts syphilis, and that syphilis not of a severe type, can undoubtedly be cured of his syphilis without much affecting the prognosis of the tuberculous disease. On the other hand, a patient in whom active tuberculosis is present and who contracts syphilis even of moderate severity, will undoubtedly much more quickly succumb to the tuberculous infection. This statement may be taken as axiomatic.

Landouzy, perhaps one of the greatest of phthisiologists, is impressed by the element of chronology in these mixed cases; that is, the age of the patient as well as the stage of the syphilitic or tuberculous disease. It can thus be seen that many permutations can be formed when the two diseases are combined. The tuberculous disease may be of the chronic, fibrotic, comparatively benign type, or it may be of the so-called "galloping" type with its rapid destruction of lung tissue and early death, even under the most favorable surroundings and the most skillful treatment. Of the first type,

that is the fibroid type, Landouzy is of the opinion that it is often possible that the disease had its origin in a long antecedent syphilis because of the sclerotic tendencies which syphilitic lesions show after the active lesion has healed. The eminent French clinician, Sergent, also calls attention to this fibroid type of tuberculosis in conjunction with aortic disease, leucoplakia, pupillary anomalies and other signs of ancient syphilis.

With Landouzy and Sergent I agree. Aside from the active phthisis seen in young syphilitics and commencing in the secondary stage of the luetic disease, tuberculosis, except in the fibroid and essentially chronic form, is rarely seen in tertiary syphilis. I will go so far as to say that tuberculous disease even of the fibroid type is comparatively rare in the tertiary syphilitic. I will give two reasons for this—two reasons which the reader will realize are pathologically sound. One is the well-known predilection of the treponemata for the vessel walls and the consequent arteriosclerosis arising therefrom. Now one of the inevitable results of this arterial hardening is high blood-pressure, which in turn causes cardiac hypertrophy to develop. Phthisis pulmonalis is essentially a disease associated with low blood-pressure. High blood-pressure in a patient with pulmonary tuberculosis is decidedly a *rara avis*. High blood-pressure and cardiac hypertrophy are antagonistic to tuberculous disease. The reason for this is not hard to find. This condition, as is well known, invariably causes more or less hyperemia—let us not say stasis—in the lungs which, as has been pointed out by Bier, absolutely counteracts tuberculous disease of the lungs. If with this we include interstitial nephritis, which is also caused by tertiary syphilis more often than is usually supposed, and which is also almost always a concomitant of the two cardiovascular conditions named, we have two very powerful reasons why tubercular disease of the lungs is comparatively rarely encountered in old tertiary syphilis—that is, in a syphilis which has existed for fifteen years or more. For these reasons, except the fibrotic form, which I believe is often inaugurated by the luetic disease, active cavity forming tuberculosis is met with extreme rarity in those affected with tertiary syphilis.

CHAPTER XXXV.

SYPHILIS AND THE CIRCULATORY SYSTEM.

The Treponema pallidum shows a very special predilection for the circulatory system—almost as much, I may say, as for the nervous system. This pathological fact has only been completely recognized within a comparatively recent time. Disturbances, which were once classified under the generic and ignorance-cloaking terms of idiopathic, we now know to be syphilitic in so far as their causative factor is concerned.

Heart.—In its attack upon the circulatory apparatus, syphilis produces many conditions which, in the light of the newer knowledge, should always cause suspicion as to its presence. Let us first consider the heart itself—the great central pumping station, as it were—which is the motive force that sends the blood coursing through the body. That syphilis attacks the heart has been known since the days of Anstruc and Morgagni—more than two hundred years ago. This early knowledge was later added to by Corvisart, Laennec, Bertin, Bouvillard and others. In 1856 Ricord wrote a classical description of cardiac gumma, and ten years later Lancereaux wrote a monograph which added much to that already described by Ricord. The observations of Fagge, Mracek and Kundrat summed up all that we knew for the forty years that followed, until the discovery of the Treponema pallidum by Schaudinn and Hoffman in 1905. Since then the work of Warthin and others has definitely established the intimate relation that frequently exists between the infectious dyscrasia, syphilis, and the pathologic processes grouped under the embracing term of heart disease.

One reason for not associating syphilis with cardiac disease more often than the facts at our command have warranted, is because as a rule these lesions do not appear until late in the disease; and until the discovery of the Wassermann reaction it can be readily understood how this could be overlooked. Even today, our knowledge of this phase of lues is asscertained largely through autopsies.

Syphilis attacks the pericardium, the myocardium and the endocardium.

Pericardium.—When the disease attacks the pericardium it is usually in the form of a fibrous pericarditis. A small patch may be

the only involvement or the entire pericardial membrane may be involved. Gummata of the pericardium are rare but when they occur they usually show themselves as small tubercles scattered over the surface. Powers and Murphy mention an unusual form in which the pericardium is thickened and adherent and the vessels thereof show numerous small aneurysms. This last I have never encountered.

Endocardium.—Syphilitic endocarditis differs from the rheumatic form in that the valves are only rarely affected. The endocardium of the left ventricle and the septum are the parts most frequently affected. In view of this fact, and also because, if the valves are affected it is usually but one and also only one cusp, syphilitic endocarditis is not as a rule as severe as the rheumatic form. It must not be forgotten, however, that syphilis in this situation may lead, although slowly, to serious effects. The walls of the heart—the musculature—may become involved, with a consequent weakening of the ventricle, and so give rise to a bulging or aneurysm formation, which may burst and death immediately ensue from hemorrhage into the pericardium; or a gummatous infiltration may cause ulceration, a thrombus or an embolus.

Myocardium.—Syphilitic myocarditis may occur either as a fibrous or as a gummatous form. In the fibrous form owing to round-cell proliferation and infiltration of the vascular connective tissue, an endarteritis obliterans results and the muscle fibers atrophy from pressure of the proliferation, and also because they are starved of their nutriment by the obliteration of the bloodvessels supplying them. The muscle fibers so destroyed are replaced by fibrous tissue and thus a cardiac fibrosis with its attendant symptoms is produced.

In gummatous myocarditis any part of the musculature may be affected, but usually it is confined to the ventricular walls and the septum. Frequently the coronary arteries are affected with an endarteritis obliterans as part of the gummatous process. As a result of this hemorrhagic infarcts of large size may form.

To Warthin of Ann Arbor we owe much of our present knowledge of cardiac syphilis. He has conclusively proven that the Treponema pallidum causes both parenchymatous and interstitial inflammation of the organ. The pericardium and the endocardium may be involved separately or together, or there may be a simultaneous involvement of the pericardium, the endocardium and the myocardium. The parenchymatous inflammation ends in fatty degeneration, simply atrophy, necrosis or pale degeneration. The interstitial inflammatory changes lead to edema, vascular and perivascular infiltration, myocarditis or gummata. Usually the parenchymatous inflammation is distinct from the interstitial;

but where there is much interstitial inflammation the parenchyma is in most instances also involved. Inflammation of the parenchymatous type indicates a virulent form of the disease, whereas the interstitial type is indicative of a mild and prolonged process which includes vascular and perivascular changes.

Strange as it may seem, the Treponema pallidum may be found in abundance in the cardiac tissues and yet be absent in other parts of the body. The organisms exist, as it were, in a latent state and may give rise to no pathologic disturbance, evidenced either by microscopic or macroscopic appearance. Since it is well known that myocardial degeneration not infrequently occurs without any assignable cause, it would seem plausible from the foregoing facts that syphilis plays a part in causing this condition that is more important than is usually supposed. In autopsies on children dying from congenital syphilis many evidences of cardiac lues are frequently found. Yet, strange to say, clinical signs are often wanting during life.

In adults, however, the pathologic types revealed at autopsy are always reflected clinically. A proper understanding of them, therefore, is of value in diagnosis and prognosis.

Myocarditis.—Chronic interstitial myocarditis begins with a perivascular infiltration in which small nodes of granulation tissue appear; later these undergo cicatricial changes, which may even go on to caseation or calcification. After a variable period of time the muscle fibers atrophy and are replaced by fibrous tissue and this neoplastic tissue may become hyaline or myxomatous. This fibrosis, it must be understood, does not necessarily imply a complete involvement—some areas always escape, notably the auricles and the papillary muscles, while the left ventricle usually suffers more than the right.

Coronary Arteries.—Another and quite common type is that of an obliterating endarteritis of the coronary arteries. If only a terminal twig is blocked an anemic infarct may result, which is followed by a local necrosis. But where the obliteration is progressive in a number of vessels simultaneously, degeneration of the cardiac musculature and interstitial inflammation naturally take place. As a result of this the cardiac wall may become so weakened that a cardiac aneurysm forms into the left ventricle as an inevitable consequence. Gummatous myocarditis is sometimes met with, but it is quite possible for a gumma of the heart to exist entirely without symptoms. It is natural to suppose that in cardiac syphilis the vessels are more or less involved. This involvement is as an endarteritis or a periarteritis. Of the two, endarteritis is more frequently met with in acquired syphilis, and periarteritis in the congenital form of the disease. It must not be overlooked,

however, that the most severe myocardial disease may show no changes in the arteries whatsoever.

Chronic interstitial myocarditis usually progresses insidiously and is frequently not recognized until the heart is in exceedingly bad shape. When death occurs it is always suddenly. The same is true when death occurs from cardiac gumma. Osler doubtless had this in mind when he said: "The frequency with which cardiac syphilis terminates the life of the patients by sudden death is remarkable."

Cardiac Syphilis.—It is often only by indirect evidence that the cardiac disease can be traced to lues. For it must be distinctly remembered that the symptomatology of cardiac syphilis cannot be distinguished from the cardiac dystrophies arising from other causes. The diagnosis, therefore, depends upon two factors—the recognition of the cardiac lesion and the presence of syphilis. The patient may, and not infrequently does, present himself to the physician quite ignorant of the fact that he has syphilis. Again, the heart may be found to be involved in a patient who is suffering from syphilis in some other part of the body. Satterthwaite found that about 5 per cent of his cardiac cases were syphilitic, and his opinion is that 10 per cent is nearer to the correct percentage. I agree with him in this opinion. Yet it is extremely difficult to state the absolute frequency of cardiac syphilis. But as a rule the skillful clinician can diagnose the condition with reasonable certainty. The general vascular changes which syphilis gives rise to are also accompanied with evidences of functional as well as organic disease of the heart. Cardiac syphilis can therefore be assumed with almost absolute certainty where we find arteriosclerosis, coronary sclerosis or sclerosis of the ascending aorta. We now know that aortic aneurysm is in nearly every instance of syphilitic origin, and where the beginning of the arch is affected (which almost invariably is the case), there are always secondary changes in the coronary arteries which produce the symptom-complex of angina pectoris. This involvement of the coronary arteries, however, is a separate entity from the periarteritis and endarteritis of the smaller vessels of the heart muscle. I may say, that this predisposition of syphilitics to coronary disease has been pointed out by Rhomberg, and with him I am in accord. There is undoubtedly a close relation between cardiac syphilis and tabes and other forms of spinal and cerebral syphilis. This fact, I think, is not sufficiently recognized. The cardiac symptoms as a rule come on after the appearance of the nervous symptoms. As a rule the nervous symptoms predominate and the cardiac lesion is often found only by accident or when the chest is examined. The cases of sudden death occurring in tabes are undoubtedly due in the majority of cases to the dilatation resulting

from myocardial degeneration, coronary thrombosis or the rupture of an aneurysm.

As is to be expected, cardiac syphilis is most frequently found in young and middle aged individuals who give no previous history of rheumatism or any of the exanthemata. Especially should cardiac syphilis be suspected in the presence of a positive Wassermann occurring in such an individual.

Clinically cardiac syphilis may show as failure of the right heart, in which there is edema, dyspnea, orthopnea, diminished urinary secretion, enlargement of the liver and edema of the lungs. It may show as failure of the left heart, in which there may be headache, giddiness, and gradual enfeeblement of the body. When the affection is chiefly myocardial there are anginoid attacks—palpitation, stitch in the side, pain over the precordium or the abdomen. Syphilis of the heart may be manifest clinically by Stokes-Adams' disease. Where there is bradycardia and attacks of vertigo it is always wise to inquire as to the possibility of syphilis being the underlying factor.

It is well to note in cardiac syphilis that subjective symptoms play an important part. These are palpitation, oppression, vague pains in the cardiac region accompanied with anxiety, in other words, all degrees of symptoms up to angina pectoris, which may be the first and for a long time the only symptom. Many cases of cardiac syphilis display psychic symptoms, such as depression bordering sometimes on melancholia, a feeling of impending death and a fear of paralysis or dementia.

Arteries.—Syphilis attacks the arteries either in localized areas of degeneration, as in the aorta, or by attacking the whole circumference of the tube as in the smaller arteries.

The most frequent expression of syphilitic disease of the blood-vessels, aside from the generalized form, is aortitis. The process begins as a round-cell infiltration following the course of the vasa vasorum, which causes a swelling and increase of the cells of their walls. There is thickening of the intima and destruction of the elastic tissue in the neighborhood of the affected vasa vasorum. There is also a fatty degeneration of the media. The Treponema pallidum can be detected in the degenerated areas. Macroscopically the changes occurring in syphilitic aoritis are very characteristic. When the vessel is opened at autopsy, small, sharply outlined plaques are to be observed. As the disease progresses these become larger and some of them merge making a placque of considerable size. In advanced cases the inner surface of the vessel has a wrinkled and scarred appearance and the patches have a yellowish gray color. In a few advanced cases there may be calcification of the degenerated areas.

The arch of the aorta is the part most frequently attacked, next in frequency is the root and then the descending portion. Contrary to the usual opinion, however, these parts of the great vessel are not the only ones affected. The thoracic and abdominal aorta are also attacked, sometimes exclusively. When the disease appears in the abdominal aorta it is in almost every instance at the celiac axis. When the root of the aorta is the site of the disease the valves are also sooner or later involved, giving rise to secondary aortic regurgitation. When the aorta is thus affected its branches, the innominate and the left common carotid, may become involved also, showing as dilatation or as true aneurysm. It is undoubtedly true that an aortitis may exist for many years without any symptoms developing. But when the aortic ring and the valves are involved a serious condition exists and one which invariably terminates fatally. It will be noted, therefore, that the location of the disease is more important than its extent.

FIG. 68.—Syphilitic aortitis. Foci about the vessels in the adventitia and media.

Clinically aortitis presents a varied picture. As I have just stated, it may be present pathologically without any clinical manifestations whatsoever. The area involved and its localization, and the presence or not of myocardial and coronary disease, are the factors that influence the clinical picture. Pain is the most prominent symptom. It is present in nearly every instance. Dyspnea is also a prominent symptom. Pain and dyspnea associated with a positive Wassermann in a middle aged subject should always cause the physician to suspect aortitis. The pain may be constant or intermittent. It increases as the disease progresses. While this pain is always present, its location is often variable. Usually it is felt most beneath the sternum. It may be felt, however, over the

entire chest or in the extremities, the neck, head, back, or abdomen. It may be felt only upon pressure either light or heavy. In some instances the symptom of pain is preceded for a considerable period by dyspnea. As a rule the two symptoms go together. This respiratory distress increases as the disease advances. It is always made worse by exercise. This dyspnea is similar to that observed in bronchial asthma in which there is a prolonged low-pitched expiration. This symptom is very typical.

Along with these two most prominent symptoms there is apt to be palpitation, hoarseness, irregular heart action, general weakness, gastric disorders, and at times fever. In aortitis there is less apt to be pulse irregularity or tachycardia, as is often observed in myocardial disease. There is an increased pulsation in the carotids and in the episternal notch, which may be noted by inspection, or the pulsatory thrill may be obtained by palpation. The tactile sense may also note a sclerosis of the superficial arteries. The heart tones show the presence of adventitious sounds. The first sound of the heart is rough. The systolic sound may be over the aortic area or it may be removed some distance away, as to the left of the sternum in the third or fourth interspace. Owing to the presence of a slight degree of pericarditis a dry, rubbing sound may at times be heard over the aortic area. The blood-pressure is not as a rule increased. This is a sign of some diagnostic value.

Aneurysm.—The relation of syphilis to aneurysm has long been recognized. This is because of the fact that aneurysm follows arteriosclerosis and aortitis, which we now know to be caused in nearly every instance by lues. Aneurysm is more apt to be found in strong, muscular men who do hard physical work. The degenerative process existing in the wall of the artery predisposes to a laceration or rupture of the intima and a bulging gradually ensues, which in time constitutes an aneurysm. I shall not dwell upon the symptoms here, because an aneurysm of no matter what cause presents the same symptomatology. In doubtful cases an *x*-ray should always be taken.

Since syphilis frequently attacks the adventitia of the arteries without attacking the media or intima, it may be said that this is a special form of syphilitic arterial disease. Such indeed is the case—the so-called *periarteritis nodosa.* It is displayed as small nodes on the external arterial walls in which the Treponemata pallida have been demonstrated. At the site of the nodules there may develop minute aneurysms, with or without thrombus formation. This condition is most frequently encountered in the arteries of the brain, particularly the vertebrals, the basilar, and the arteries which go to form the circle of Willis. Where an artery is in proximity to a gumma, gummatous infiltration as a rule follows. To this process may be ascribed acute perforating ulcer of the aorta.

When the inner lining of the arteries is affected, the condition known as endarteritis exists. Usually it is obliterative, that is, the process continues until finally the lumen of the vessel is destroyed. In nearly every instance it is only the arteries of small caliber that are attacked. Usually a single system of arteries is affected—the coronary arteries, or those of the leg or the brain.

Syphilis when it attacks the arteries frequently, as would be supposed, gives rise to hemorrhage. This is to be noted in the almost invariably fatal hemorrhage of aneurysm or in cerebral hemorrhage. It is in the brain that the symptoms of syphilitic arteritis have been studied most extensively. These are transient paralysis of the hemiplegic type which in many instances, unless stayed by treatment, finally results in a hemiplegia, which is permanent, or in softening of the brain with its attendant symptoms. When the process is slower and the lumen of the arterial tube is narrowed gradually there is caused intermittent interruption of the blood supply to the part which usually terminates in thrombosis. Should this occur in an extremity, the phenomenon known as intermittent claudication results. This symptom does not occur when the muscles are in a state of rest, as the arteriosclerotic vessels are then still able to nourish them; but only after the muscles have been used and have become more or less fatigued. It is then that the pain appears. Recently Moschcowicz has made it possible to study the circulatory conditions in this affection of the vessels by means of his hyperemia test.

While not in every instance, still in a sufficiently large percentage of all cases, high blood-pressure is a concomitant of syphilis. It is not possible to study this common and interesting symptom-complex in its entirety here, except to say that in all cases of high blood-pressure under forty-five years of age suspect syphilis and—suspect it very strongly.[1]

Treatment of Cardiac Syphilis.—The treatment of cardiac syphilis is of course the treatment of syphilis in general, which will be dwelt upon in detail elsewhere in this book. But in view of the fact that the treatment of cardiac syphilis requires a certain degree of individualizing, I shall briefly review it at the conclusion of this chapter.

Unlike the results of treatment of cardiopathies arising from other causes, such as rheumatism or the exanthemata, the treatment of cardiac syphilis in many instances offers a better chance of cure. But always with this proviso: if the heart is permanently injured beneficial results will not occur beyond the amount of injury. In other words, the scars will always remain—they cannot be obliterated. As in almost all cardiac diseases, rest is absolutely essential,

[1] See "Syphilis and High-blood Pressure," by Burton Peter Thom, M. D., in Medical Record, January 21, 1922.

and those cases requiring specific treatment do best if compelled to remain in the recumbent position. Should the cardiac involvement be discovered while its luetic cause is active—which unfortunately does not always happen—heart stimulants, such as digitalis, strophanthus, caffeine, adonis vernalis, etc., as a rule give only moderate results. In the later stages—I am here referring to myocarditis—after fibrosis to a decided degree has occurred, cure is of course impossible, but digitalis and similar drugs may be given with more advantage and so to a limited extent may prolong the patient's life and make his existence, until the end comes, more comfortable. It has been observed clinically that these drugs have a more potent effect if combined with potassium iodide. But, except in relieving the pain that may accompany aneurysm, this drug is of no avail in overcoming the fibrosis once it is established. Potassium iodide acts most powerfully where gummata are present and where the deposits or exudates are of recent origin. If given as a matter of routine, which I might add in passing I do not advise, it should be given after the patient has received the full benefit of previous mercurial and arsphenamine treatment.

While arsphenamine undoubtedly occupies a most important place in the treatment of cardiac syphilis, it should always be preceded by a course of mercury. Nor should it be given then until some improvement has been observed by the administration of mercury and of some of the heart stimulants. It should not be given under any circumstances in severe, uncompensated lesions, accompanied with dyspnea and pulse irregularity, or where there is arising from the cardiopathy emphysema and chronic bronchitis and aortic or cardiac aneurysm. It is also well to remember that in giving arsphenamine the first injection is apt to be the most dangerous. Symptoms of cardiac collapse sometimes occur with the administration of arsphenamine, as Carroll and Brooks have observed. Personally I have not observed this but it is undoubtedly a contingency which must be reckoned with. I prefer giving mercury by the intravenous route; if this is not possible my next choice is by inunctions. My next preference is for the insoluble salts such as the salicylate, gray oil or Lambkin's cream. No dependence can be placed on treatment by mouth, but if for some reason none of these methods can be employed and the drug must perforce be given *per os*, I prefer that ancient but still honorable preparation known as Zittmann's decoction.

All cases of cardiac syphilis should receive persistent treatment for at least a year after the symptoms have disappeared or have been much modified. It is well to note in this connection that many of these cases, while cured from a clinical standpoint, still show a positive Wassermann. This may persist indefinitely. For it is

well known that in some instances it is practically impossible to change a positive Wassermann to a negative. A peculiar fact to be noted in a not inconsiderable number of these cardio-syphilitics is that, after apparent recovery, they suddenly die. So constant is this occurrence that it must be included in giving a prognosis.

Thus it is to be seen that syphilis of the heart itself occurs much more frequently than is usually supposed. It is needless for me to say how frequent it is where the bloodvessels are concerned. Also it is to be noted that if treated early recovery is more likely to occur than in cardiopathies arising from other causes. For that reason every syphilitic should be examined for heart lesions arising therefrom, and appropriate treatment given promptly.

CHAPTER XXXVI.

SYPHILIS AND THE ANEMIAS.

In the light of the newer knowledge of the pathology of syphilis we can believe that the blood shares with the other viscera in the general spirochetosis. I do not wish the reader to infer from this that syphilis is a septicemic infection, it is decidedly not; as an infection it is essentially metastatic. It is along the course of the lymphatics that the Treponema pallidum travels; yet their ultimate diffusion is by the blood stream. The blood stream is by no means a favorable medium for the multiplication of the parasite; experiments have shown that when the blood is used for purposes of inoculation positive results are rarely obtained. This is due to the fact that the treponemata in the blood stream are inconstant and few in number. But while the spirochetosis in the blood is relatively less than it is in the other organs, the collective influence is such that in as much as disorders of the blood are not primary but arise from metabolic derangement it is not difficult to conceive how a constitutional infection like syphilis can give rise to those conditions which we class under the generic term of the anemias.

Blood Changes in Syphilis.—The changes in the blood in syphilis occur very early in the disease and they are constant, unless treatment has been instituted as soon as the chancre has been discovered. There is at first a moderate leukocytosis which slowly increases and finally reaches its highest point with the appearance of the eruption. This increase in the white cells is only moderate as a rule, but counts as high as twenty thousand have been recorded. The cells which predominate are the lymphocytes; the polymorphonuclear cells are increased but not to the extent observable in sepsis. The eosinophiles are also increased although this is denied by Peter. According to Rille the increase in the number of eosinophiles is particularly noticeable in papular eruptions. I have not had opportunity to confirm this but the analogy of other skin disorders to syphilis leads me to believe that it is true. Iodophilia is sometimes observed but it is by no means constant. The same can be said in regard to the presence of blood plaques. In 1904, Ravaut called attention to the fact that coincident with the circulatory leukocytosis the cellular elements in the cerebrospinal fluid are also increased. This has since been confirmed by both American and foreign observers.

The first study of the erythrocytes or red blood cells in syphilis was made by Grassi more than sixty years ago. Later investigators studied the effect of the disease upon the hemoglobin. Of these, Stoukovenoff and Konried did work that is still authoritative.

Changes in Red Blood Cells.—If the first change in the blood in syphilis is a beginning leukocytosis the second is a decrease in the number of the red blood cells. Not infrequently it is coincident with the leukocytosis. With the decrease in the number of red blood cells there is a decrease in the amount of hemoglobin. Unless checked by treatment this decrease in the red blood cells and the hemoglobin continues, sometimes slowly, sometimes rapidly, and reaches its maximum intensity when the eruption appears. It usually remains stationary during the eruption and when the eruption has disappeared gradually returns to normal. The fall in the number of red blood cells is rarely below four million; whereas the fall in the hemoglobin percentage is from 20 to 30 per cent or even more. Thus it will be seen that the anemia of syphilis is a true chloro-anemia; that is an anemia that is a true impoverishment of the blood in that the hemoglobin and consequently the color index are lowered out of proportion to the lowering in the number of red blood cells. In quite a few instances however, the diminution in the number of red blood cells and the amount of hemoglobin is strictly proportionate—this constitutes simple anemia. Most text-books state that chloro-anemia is the anemia typical of syphilis; I am not altogether in accord with this, but incline to the opinion that the anemia most frequently encountered in early syphilis is of the simple type.

Anemias of Syphilitic Origin.—The blood changes just described are rarely permanent and are readily amenable to treatment. In fact, if treatment is begun as soon as the chancre has been diagnosed they hardly, if ever occur at all. In the tertiary stage however, anemias resembling those of the graver type sometimes occur. The word "resembling" being used in a modifying and restrictive sense in that these anemias of syphilitic origin parallel the others only in their hematology and symptomatology and not in their pathologic cause, except in so far as syphilis is the factor, and in their outcome, which in the majority of instances is much more favorable when due to syphilis. The reader will perhaps, grasp my meaning better when I say that these graver anemias can all be simulated by syphilis in the tertiary stage.

Pernicious Anemia of Syphilis.—The most frequent of these grave anemias which syphilis simulates is pernicious anemia. The pernicious anemia of syphilis does not differ in so far as the changes in the blood and the symptomatology are concerned from the Addison-Biermer type of unknown origin. It has been stated that

the condition is more frequent in women than in men. That may be so if due to some other cause than syphilis, but cases of syphilitic origin are undoubtedly more frequent in men than in women.

The onset is insidious; the patient feels weak and is easily fatigued without apparent cause. This weakness may be the only symptom for a while but gradually anorexia, headache, dizziness, ringing in the ears, shortness of breath and troublesome dyspeptic symptoms develop. Fever is frequently present and in many instances leads to errors in diagnosis in that it presupposes some focus of pyogenic infection. As in all severe anemias petechiæ and ecchymoses are frequent and disturbances of vision due to retinal hemorrhage are not uncommon. The complexion gradually assumes a yellow, shiny appearance, that to the experienced eye is characteristic. Not infrequently these patients are plump rather than thin. Cardiac murmurs and dyspnea are frequent—these murmurs however are distinctly hemic and care should be taken to distinguish them from those occurring in subacute endocarditis. Swelling of the feet and ankles is often observed.

The liver is frequently enlarged and this enlargement together with the lemon colored complexion may cause a diagnosis of hepatic disease to be made. This error is rendered still more probable by the high colored urine due to the presence of bile salts. Since gastric pain and disturbances of digestion are frequent together with enlargement of the liver and a lemon colored complexion, carcinoma is not infrequently suspected—especially since the condition occurs at the age when malignancy is met with. Symptoms referable to the spinal cord are also not uncommon. These may resemble tabes or spastic paraplegias.

The blood picture shows a marked reduction in the number of the red blood cells. As a rule they number about two million per c.mm., but they may be reduced to below two hundred thousand. The blood may show macrocytosis and poikilocytosis if examined fresh. In stained preparations nucleated red blood cells are invariably present and many of them are polychromasic and many of them show basophilic granulation. Normoblasts and megaloblasts are also seen. The hemoglobin content is diminished but not in proportion to the number of red blood cells. The color index is high—usually more than 1 and not infrequently 1.5. The white blood cells show a moderate leukopenia; the polymorphonuclear, the eosinophiles and the large mononuclear cells being especially lessened. The absence of these cells is replaced by lymphocytes, but the increase in these latter is relative rather than actual. The blood platelets are usually diminished. The total amount of blood is diminished to a considerable degree. The coagulation time is increased and the water content of the blood is increased. The viscosity and the specific gravity are low.

Syphilitic pernicious anemia is nearly always curable. Syphilis as a cause is more frequent in my opinion than is usually supposed. For that reason, when encountered the possibility of a syphilitic origin should always be considered.

Secondary Anemia of Syphilis.—In the tertiary stage of syphilis, especially in patients debilitated from any cause including the disease, secondary anemia frequently develops. The syphilitic cachexia sooner or later induces a hypoplastic condition of the bone marrow, which in some instances is augmented by actual syphilitic bone disease of prolonged chronicity. While extra-medullary erythropoiesis in the liver and spleen may continue to supply in part the needed erythrocytes, these organs also may be affected by the dyscrasia and their activity impaired, so that they are unable to make up the loss caused by the atrophy of the bone marrow.

In these cases the number of red blood cells is diminished and the hemoglobin is also diminished and in a greater proportion than the red blood cells. The color index is usually below 1, although it may be normal. Leukocytosis of a moderate degree is often present, the neutrophile cells being in excess. Leukocytosis is especially apt to be present if there is intramedullary gumma, the existence of which may in some instances be determined by the *x*-ray.

This form of anemia is in my opinion extremely common in tertiary syphilis. It is more frequently encountered however, in that class which makes up the population of prisons and pauper institutions—the flotsam and jetsam of humanity deep bitten with the disease through neglect, alcoholism or drug addiction. The sallow or rather earthy color of the skin of many patients with old, uncared for syphilis enables one accustomed to seeing large numbers of them to diagnose their disease with almost unfailing accuracy. Myelopathic anemia due to syphilis readily responds to treatment and improved hygienic surroundings. It is often remarkable to observe how these patients pick up when given a few injections of arsphenamine and good food and fresh air.

Vaquez's Disease.—Vaquez's disease or Osler's disease, by which is meant an erythemia or an increase in the number of red blood cells and in the quantity of blood due to a hyperplasia of the erythropoietic tissue can in some instances I believe, be traced to syphilis. It is comparatively rare, but it is these rare and bizarre conditions that should always arouse suspicion of syphilis for the reason that tertiary syphilis never goes by rule but often attacks in ways unthinkable.

Leukemia.—Leukemia is a comparatively rare disease of unknown etiology. I am in accord with Barker that in some instances it may be due to syphilis. In any event every case of leukemia should

have the benefit of a Wassermann test, which if positive should be followed by arsphenamine therapy. Leukemia is not as was formerly believed a disease of splenic origin. It originates either in the myeloid tissue of the bone marrow or in the lymphadenoid tissue which is distributed all over the body; hence there are two types—the myeloid and the lymphadenoid, both of which may be acute or chronic. The chronic myeloid type is that which is most frequently encountered.

Chronic Myeloid Leukemia.—The disease is characterized clinically by a slowly increasing weakness, pallor and enlargement of the spleen. There is also abdominal pain, usually on the left side, palpitation, dyspnea and sometimes hemorrhages into the retina, or labyrinth, or epistaxis. The spleen is enormously enlarged. It may or may not be tender. The liver is also enlarged. The bones, especially the sternum and ribs are tender to pressure. The lymphatic glands are also enlarged. In addition to this, irregular fever and night sweats are nearly always present. Constipation is usual; it may alternate with attacks of diarrhea.

In the beginning the number of red blood cells and the percentage of hemoglobin is not much diminished but as the disease progresses there is a marked fall in both. The white blood cells are enormously increased; ranging from one hundred thousand to half a million per c.mm. Of these the myelocytes predominate. Myeloblasts are also present in considerable numbers, also transitional forms between them and the myelocytes. The blood platelets are usually increased. The volume of blood is increased. The coagulation time is increased. The fibrinogen is diminished.

Acute Myeloid Leukemia.—Acute myeloid leukemia resembles clinically an acute, virulent, infectious febrile disease. It is characterized by high continuous fever, hemorrhages and a rapidly developing anemia. It is rare, and I can find no reference to syphilis as a probable cause in the literature. It is one of the few diseases I believe, which syphilis never simulates.

Chronic Lymphadenoid Leukemia.—Chronic lymphadenoid leukemia is not as frequent as the chronic myeloid type. It is the type however which I believe to be most frequently caused by syphilis. With certain exceptions which will be enumerated the objective and subjective symptoms do not differ from the myeloid type. Lymphadenoid leukemia is characterized by a generalized enlargement of the lymph glands. This glandular enlargement is not great—not so marked by any means as in Hodgkin's disease, but considerably more pronounced than the glandular enlargement in active secondary syphilis. The tonsils are also enlarged and occasionally lymphoid nodules can be felt in the skin. The spleen is enlarged but not as much as in the myeloid type. The liver is also enlarged

but not to any marked degree. In some instances however there is no glandular enlargement visible and the disease is determined by the blood picture alone. In such cases it is to be inferred that the deeper glands are those that are hyperplasic. Fever and albuminuria are sometimes present.

As in the myeloid type the red blood cells and the hemoglobin are reduced. The increase in the white blood cells also averages the same; that is, between one hundred thousand and a half a million, the increase being in the small mononuclears or lymphocytes. The polymorphonuclear, large mononuclear, and transitional cells, represent only a small percentage. As pointed out by Morawitz there is a uniformity in the leukocytosis of this type of leukemia that is characteristic. This uniformity consists in the overwhelming predominance of the small lymphocytes as contrasted with the greater cellular variety of the myeloid type.

Acute Lymphadenoid Leukemia.—Acute lymphadenoid leukemia is clinically not unlike a primary sepsis that extends over several months. Fever, headache, pains in the limbs and vomiting are the opening symptoms. There is often difficulty in swallowing and owing to the gums often becoming spongy there is pain in the mastication of food. The tonsils are usually enlarged and covered with a whitish exudate. At first there may be no lymphatic enlargement except a slight enlargement of the cervical glands; later there is a moderate generalized enlargement. The spleen does not enlarge until late. There is evidence of nephritis also in that albumin and casts are present in the urine.

The characteristic blood changes are established within a week. The red blood cells are diminished and the hemoglobin in proportion. The color index is less than 1. The predominating white blood cells, which may number from one hundred thousand to half a million, are the mononuclear cells, which may be present to as high as 95 per cent.

Since this type of leukemia nearly always occurs in children and young adults, when of syphilitic origin it can be assumed to be congenital. I do not know of its having occurred on an acquired syphilitic basis.

Hodgkin's Disease.—Hodgkin's disease is an infectious granuloma of the lymph glands. I am in accord with Irons that it is probably due to a diphtheroid bacillus. It cannot be denied however, that in some instances syphilis—nearly always congenital—can exactly simulate its clinical display. For that reason the condition is described here. The process is encountered most frequently in children at or a few years before puberty. Males are more frequently affected than females. The lymphatic enlargement is the first symptom noticed. Usually this is in the glands of the neck,

although the glands of the groin, axilla, or of the mediastinum may first show involvement. If the mediastinal glands are first involved the child will have as the first objective symptom a troublesome cough that is not relieved by ordinary remedies. As the disease develops the patient's bodily strength and appetite fail. He is easily fatigued and suffers from shortness of breath after slight exertion. Nearly always there is a progressive loss of weight but this may not be observed until the disease has made considerable progress. Owing to the anemia there is pallor and in very many instances the patient complains of a generalized pruritus, and cutaneous eruptions of various kinds are not uncommon. Fever of a relapsing nature is nearly always present. The patient's temperature may be normal or subnormal or only raised to a slight degree when suddenly a temperature of five or six degrees above normal develops. This lasts for a few days and then slowly declines —the febrile period having lasted altogether about a week. This relapsing pyrexia may go on for months. In some instances the external, palpable glands are not involved, the glandular involvement being entirely internal. In such cases the peculiar temperature conditions, the marked anemia and the mental hebetude are clinical features that should merit consideration in making the diagnosis.

Anemia is not present early in the disease but it soon develops and may reach a high grade. The blood picture therefore presents a reduction in the number of red blood cells and in the amount of hemoglobin; the proportion of which is reduced more than the red blood cells. Leukocytosis is not present at first but later develops to a moderate degree—the cell count rarely exceeding forty thousand cells. The polymorphonuclear cells are increased. The eosinophiles are increased very much in some cases and diminished in others. Transitional forms of mononuclear cells are frequently seen. Histologic examination of the lymph glands if excised during life shows the presence of fibroblasts, megaloblasts and eosinophiles.

Since fibrinogen—the coagulative substance in the blood—is invariably diminished in infections that work injury to the hepatic cells, and since the Treponema pallidum, especially when transmitted congenitally, shows a decided tendency to attack this organ, it is therefore reasonable to presume that diseases in which the coagulability of the blood is disturbed—hemorrhagic diseases—should have syphilis in many instances as the underlying causative factor.

Hemophilia.—Whether syphilis in some remote ancestor was the starting point of the condition known as hemophilia in which the coagulability of the blood is diminished it is impossible to say. I believe it probable however. Fatal hemorrhage from the umbilicus

is not infrequent in new-born syphilitic infants and it would seem to me that there is a close analogy between this and the hemophilia of childhood and early adolescence.

Purpura.—Purpura, in some instances, can undoubtedly be traced to congenital syphilis when occurring in children. In adults this is problematical but I believe it to be possible.

Paroxysmal Hematuria.—The rare condition known as paroxysmal hematuria in which, usually after exposure to cold or getting the feet wet, the urine suddenly becomes dark red due to the presence of oxyhemoglobin and methemoglobin, is in many instances due to syphilis. The urine clears up within twenty-four hours but if the attacks occur at frequent intervals a moderate degree of anemia may develop. During an attack there is a reduction in the number of lymphocytes and eosinophiles and the red blood cells are distorted—poikilocytosis. During the intervals between attacks there is often present a moderate albuminuria.

As I have already stated syphilis does not produce these anemias *per se*. Rather does it produce clinical manifestations which resemble them very closely—so closely that clinically they cannot be told apart. Also, in many of these anemias—the true ones, the causes of which we do not know—the prognosis is nearly always unfavorable—they terminate in death. With the anemias of syphilis recovery often happens. Sometimes it is the only difference between them.

It is also possible that any of these grave anemias may exist in a syphilitic and yet be independent of the syphilis. Arsphenamine helps these patients—it helps in all anemias, whether syphilitic or not. This is a fact to be remembered.

CHAPTER XXXVII.

SYPHILIS OF THE BONES AND JOINTS.

That syphilis attacks the bones with great frequency and to a lesser degree, the joints, has long been recognized. This applies to the congenital form of the disease as well. Syphilitic osseous lesions which also involved the articulations were mentioned by Villobos in 1498; also by Fracastor, Ambrose Pare, and Della Croce in the sixteenth century. In 1791, John Hunter described syphilitic periostitis and expressed the opinion that cold and exposure were factors, in addition to the constitutional dyscrasia, in producing it. He also pointed out that the bones most liable to be affected were those nearest the surface of the body—the tibiæ and the calvarium. These lesions of the osseous system were first described with scientific accuracy however, by Lancereaux in the sixth decade of the last century. Since then and particularly since the introduction of the roentgen ray our knowledge of bone syphilis has greatly advanced and an extensive literature on this phase of the disease has accumulated.

Early Joint Involvement.—In the early stages of syphilis, even before the disappearance of the chancre in some instances, fully 5 per cent of all patients complain of arthralgia—pain in the joints. This arthralgia may be monoarticular or polyarticular—usually several joints are involved. The knee, elbow, ankle and wrist are the joints most often affected. The pains are almost invariably worse at night and may be so severe as to simulate those of acute articular rheumatism. They are to be differentiated from acute articular rheumatism however, in that they are entirely subjective, not being accompanied with heat, redness or swelling of the part affected, nor is fever present, unless it be the low evening rise of temperature sometimes observed in early syphilis. It is also characteristic of this syphilitic arthralgia that the pains are diminished by motion. They are absolutely uninfluenced by salicylates.

Osteocopic Pain.—Concomitant with the arthralgia the patient frequently complains of "pains in the bones." These are the osteocopic pains which may be regarded as pathognomonic of the disease in the secondary stage. Like the arthralgia they are invariably worse at night. Many times in fact they are not present during the day at all but occur promptly as soon as the patient goes

to bed. These pains are due to a periostitis and the bones affected may transmit a cutaneous swelling and redness and tenderness on pressure. The tibiæ, "the bone that syphilis loves," the clavicles and the bones of the cranial vertex are those most frequently involved. It is these bones also which are most frequently affected by tertiary lesions. Bradrick and Mauriac have also called attention to the comparative frequency of the "heart pain" complained of at this period, which is nothing more than a periostitis of the sternum. This sternal periostitis is often accompanied with shortness of breath upon exertion.

Early Bone Involvement.—When syphilis attacks the osseous structures in the early phase of its evolution it also causes more or less impairment of the general health. This is exemplified by the analysis of 165 cases of early secondary syphilis made by Wile and Senear. They observed involvement of the osseous structures in 60 cases. Of these, 36 showed some definite constitutional disturbance in addition to the osseous lesion. Thus, in 18 the general health was severely affected as evidenced by marked anemia, loss of weight, debility and anorexia. Eight showed the same only to a less degree. Ten showed only a slight loss of weight and slight anorexia. The remaining 24 were not affected in their general health. From this analysis the authors named concluded that involvement of the skeleton reflected a more or less toxic effect on the body as a whole. I am in accord with their experience. This early involvement of the osseous structures, unless met by energetic treatment, always presages a severe infection, not only in the secondary stage but also in the tertiary. There does not seem to be any correlation between the exanthemata of the secondary stage and these bone lesions. In fact, the exanthemata, are if anything, less pronounced when the bones are early involved. It has also been said that when syphilis attacks the bones it rarely if ever, attacks the nervous system. With this statement I am not in accord. On the contrary I believe that bone syphilis is not infrequently followed by nervous syphilis.

Formation of Exostoses.—The secondary manifestations of syphilis as it affects the bones takes the form of a periostitis. It is a small-celled proliferative inflammation of a low grade and consequently is never attended with destruction of the substance of the bone. If left to itself, or if not treated with sufficient vigor, this periosteal proliferation in time condenses or eburnates—that is it becomes transformed into a lamina of new bone beneath the periosteum. It is this new bone formation which in both the acquired and congenital form of the disease gives rise to exostoses. When appearing on the shins as it very frequently does it produces the characteristic outward curving of the anterior aspect of the tibiæ

known as "sabre shins" which is always pathognomonic of syphilis. If occurring on the inner table of the vertex or a canal of exit for some nerve, symptoms due to pressure supervene. Not a few nervous lesions—especially of the third and eighth nerves—are caused by the pressure exerted by this pathologic hypertrophy of bone.

Syphilitic Periostitis.—In syphilitic periostitis the swelling is uniform. It is not circumscribed, nor does it end abruptly, but gradually merges into the surrounding bone. If the bone affected is a long bone it imparts a fusiform appearance by reason of the fact that the entire circumference of the bone is involved. This helps to differentiate it from sarcoma in which the growth is sharply defined and grows from one side of the bone only. Aside from the pain, there is heat, redness and swelling over the bone if it is near the body surface. If the bone is deep seated the only symptom will be pain, usually worse at night and, possibly pressure symptoms if the process involves the periosteal covering of the lumen of a bony canal. Sometimes, but not often, periostitis may occur in the tertiary stage. In such instances the inflammation extends downward and involves the bone substance causing osteitis or osteomyelitis and unless checked may result in considerable destruction.

Synovitis.—Coming on somewhat later than the arthralgia mentioned as occurring in the first few weeks or months of the infection, an acute synovitis may occur. It most often affects one knee, but is not limited to any particular joint. The synovial membrane is infiltrated and thickened and the joint is stiff on motion and more or less painful—although the pain is never intense. There may be some slight edema about the joint. Under treatment the condition soon disappears; however, if untreated it may become chronic, fimbriæ may form in the joint and the consequent irritation may cause considerable effusion giving the joint an appearance not unlike that of *tumor albus* or "white swelling" of tuberculous disease. It can be distinguished clinically from the last, however, by the following: In syphilitic disease there is never any wasting of the part above or below the swelling; in tuberculosis there is always more or less atrophy present; pain is not prominent in syphilis whereas in tuberculosis it is; motion is not impaired or only slightly so in syphilis; in tuberculosis there is invariably more or less—usually more—impairment of motion. In passing I wish to add that while this condition is usually met with in the late secondary stage of the disease, it is not infrequently encountered as a tertiary manifestation.

Gummata of Bone.—The conditions I have just described—the arthralgias and osseous lesions of the secondary stage are in nearly every instance easily amenable to treatment and pass leaving hardly,

if any, trace. They are as ephemeral as the secondary exanthemata, to which in a measure they may be likened. In the tertiary stage there is a different story to tell. The characteristic lesion of the tertiary stage—the gumma—now enters upon the scene. As in the periostitis of the secondary stage the bones most frequently affected are those superficially situated—the tibiæ, the clavicles, the carpals and metacarpals and those of the cranial vertex. Gummata of the bones may begin either in the periosteum or in the interior of the bone. If the gummatous infiltration begins in the periosteum it assumes in the beginning the appearance such as is noted in the periostitis of the secondary stage. But the process does not stop at this. It dips into the bone beneath and causes osteitis or osteomyelitis with consequent necrosis. The overlying cutaneous surface ulcerates exposing the diseased bone beneath. This may separate as a sequestrum and have to be removed surgically, or it may work its way to the surface through a sinus. In this way the destruction of osseous tissue may be very great and fracture, if a long bone is involved, or deformity, if of the bones of the nose, may result. Gummatous periostitis of the bones forming the vertex of the cranium may result in perforation involving the dura mater and the underlying brain. In most instances of this kind however, the dura mater limits the process and the necrosed bone is discharged externally. This gummatous infiltration does not always begin in the periosteum but in the cancellous portion of the bone causing it to become obliterated. The bone in consequence becomes thickened and much more dense and heavy than normal. When seen by the roentgen ray this density can be easily detected and is a most important feature in differentiating syphilis from the rarefaction and consequently fainter shadow of tuberculosis. This form of tertiary syphilitic bone disease not infrequently attacks the femur and when it occurs in a comparatively young adult in the absence of other signs of syphilis or where the disease is not suspected, may suggest incipient tuberculosis of the hip-joint, as the symptoms of slight pain, heaviness and easy fatiguability referred to the affected part are clinically much the same. In all of these cases along with the destruction caused by the gummatous infiltration healing by eburnation takes place concomitantly, so that where destructive ulceration exists in one part of the lesion another part is healing by the condensation of the products of the inflammation. In this respect syphilitic bone disease differs from tuberculous bone disease in which there is no tendency to new bone formation.

Gummata in Bone Marrow.—As pointed out by Chiari, gummata may form in the bone marrow. They frequently give rise to no subjective symptoms, or objective signs are found only at necropsy. When so found they appear as yellow gelatinous masses, single or

entirely filling the marrow cavity. If the neoplasm grows unchecked it in time bulges the cortex of the bone causing it to become spindle-shaped or fusiform. The cutaneous covering may break down and sinuses result but from these no sequestra will be extruded.

Syphilis and Tuberculosis.—Tertiary syphilis of the bones is most frequently mistaken for tuberculosis or sarcoma. Tuberculosis in particular is sometimes simulated so closely by syphilis that it is clinically impossible to diagnose between them. The diagnosis in not a few instances is still further complicated by the presence of a positive Wassermann reaction. It must not be forgotten that syphilis and tuberculosis as two separate disease entities can exist in the same body. It is also my opinion that not infrequently, in fact more often than is usually supposed, the two infections coexist in the same lesion. I believe that this happens not infrequently in the vertebral column. It was formerly taught in text-books and in the lecture halls that syphilis rarely attacked the vertebræ. The more recent observations of Hunt, Whitney and Baldwin, and Fordyce have proved conclusively that the spinal segments are far from being exempt from syphilitic bone disease. Tuberculosis of the bones of the spinal column is characteristic and will not be discussed here, but if in conjunction with a positive Wassermann reaction there is with the localized immobilization hypotonicity of the ligaments and muscles of the bones not involved, including the sacro-iliac articulations, syphilis as a complicating factor can be diagnosed with almost absolute certainty.

Gumma and Sarcoma.—Gummata of the bone may be mistaken for sarcomata clinically. It a fact not generally known that sarcomata, even in the absence of syphilis, sometimes give a positive Wassermann reaction. As a rule however, their growth is much more rapid than even that of a rapidly developing gumma but in the absence of other confirmatory signs of syphilis, or if there is still a doubt clinically even with a positive Wassermann reaction, resort must be had to the microscope to determine the nature of the process.

Conditions which may be Mistaken for Tertiary Syphilitic Bone Lesion.—Tertiary syphilitic bone disease may be mistaken for septic periostitis or osteitis or osteomyelitis; especially if the patient has recently recovered from typhoid fever, although it must not be forgotten that osteomyelitis, particularly of the ribs, frequently follows typhoid fever and may thus occur independently of the syphilitic infection. It may be mistaken for actinomycosis or actinomycosis may be mistaken for syphilis. The presence or absence of the ray fungus will determine the diagnosis. In the subtropical East mycetoma or "Madura foot" may be mistaken for syphilis. The presence or absence of the characteristic granules will

determine the diagnosis. New growths such as fibroma, chondroma, osteoma may cause a suspicion of syphilis; in case of doubt a Wassermann test should be taken.

Tertiary Syphilis of Joints.—In the tertiary stage syphilis sometimes attacks the joints. Strange to say this was denied by Ricord, but in 1853 his contemporary, Richet reported a case of gummatous arthritis. Ten years later, Lancereaux described a case seen at necropsy. Shortly after Fournier reported a series of cases and since that time many observers have seen and reported the condition. Gummatous joint disease is in almost every instance a very late tertiary manifestation. This means that it is most apt to occur during middle life or later, which from the standpoint of age incidence goes far in eliminating tuberculosis in the differential diagnosis.

Gummatous Involvement of Synovial Membrane.—Gummatous infiltration of the synovial membrane and of the fibrous covering and ligaments composing a joint—usually that of the knee, elbow, ankle or wrist, in the order named—may be primary or it may be an extension of a disease focus from the articular end of a bone. In most instances the process is insidious and of slow development. The patient first notices a slight pain and swelling of the joint, which is also slightly stiff. He usually attributes it to rheumatism or to advancing age. As time goes on the effusion increases and becomes intra-articular, the synovial membrane of the joint and of the tendon bursa as well and the fibrous capsule become very much thickened. Erosion of the articular cartilages takes place, thus causing crepitation on motion. The process may become stationary at this stage and remain so for years. While movement of the joint is impaired, complete ankylosis rarely occurs. In some instances however, the gummatous infiltration undergoes ulceration and the elements composing the joint may be more or less destroyed. There may be sinus formation and discharge of sequestra, and in healing, the gummatous infiltrate may condense into fibrous bands. This, combined with the destruction of the cartilaginous and osseous elements, may render the joint absolutely useless.

The syphilitic arthropathy known as Charcot's joint is discussed in the chapter on Tabes Dorsalis to which I refer the reader.

Prognosis.—The prognosis of syphilitic disease of the bones and joints depends almost entirely upon the time when treatment is begun. The lesions of the early secondary stage in many instances get well spontaneously. They invariably yield to specific treatment promptly and when cured as a rule do not return. Tertiary lesions also respond to treatment in a most satisfactory way if diagnosed early and treated vigorously. Where there has been much destruction of tissue the prognosis as to resoration of function or to the return to normal appearance is naturally poor or at best

dependent upon circumstances which it may or may not be possible to control. It is always possible however to promise the patient that the progress of the condition can be arrested.

Treatment.—The treatment of syphilis of the bones and joints is almost entirely constitutional. Removal of sequestra or curettage of a diseased bone is sometimes necessary. Effusion into a joint if of large amount may require drainage. This can usually be accomplished by puncture. It may be necessary to immobilize a joint by means of splints or a plaster of Paris cast while treatment is being administered. This procedure is of advantage in chronic arthritis to hasten the absorption of a moderate effusion and to acquire the therapeutic aid which rest affords. Adhesions may have to be broken up under anesthesia; after this is done the part should be immobilized for several days and then gently massaged, and heat applied either by hot packs or by baking.

Congenital Syphilis.—Congenital syphilis of the bones and joints is rather more atypical than in the acquired disease. Although transmissions of the disease from parent to child has been known since the time of Paracelsus, lesions of these structures of congenital form do not seem to have been frequently recognized. Even as late as 1856, Diday wrote that the literature on the subject was very scarce. To Hutchinson, Parrot, Wegner and Taylor we owe much of our present clinical knowledge of congenital syphilis as it affects the bones and joints.

Syphilitic Bone Lesions in Infants.—In determining syphilitic osseous lesions in infants the chief difficulty lies in their close resemblance in many instances to rachitis. This was the error into which Parrot fell so often, although the reinvestigation of the facts observed by him, by Sir Thomas Barlow, and Dr. Lees confirmed his observations in the main while correcting certain inferences which the more limited pathologic knowledge of his time caused him to make. As a rule the syphilitic bone lesions occurring in infants appear much earlier than those due to rachitis, nor are they dependent upon disturbances of nutrition as those of rachitis undoubtedly are. Rachitis frequently develops in congenitally syphilitic infants, but according to Holt "the connection seems to be no closer than with any other cachexia." With this I am not in accord. On the contrary, it is my opinion that congenital syphilis in many instances gives rise to a condition, particularly observable in the osseous structures, that might without any infringement of pathologic verity be termed, *rachitis syphilitica*. This by no means applies to every case of rachitis but the combination of the two diseases—syphilis and rachitis—the last determined by the first, I am convinced occurs much more frequently than is usually supposed. I would therefore suggest to the reader that in every case of rachitis a Wassermann test should be taken.

Syphilitic Bone and Joint Lesions in Fetus.—That syphilis attacks the bones and joints *in utero* is evidenced by the flaccidity of the joints, caused by the separation of the epiphyses of infants born dead at term. This syphilitic osteochondritis commonly designated as the pseudo-paralysis of Wegner is the earliest sign of congenital syphilis of the bones and joints and aside from that it is also an absolutely pathognomonic sign of the disease. It frequently precedes all other manifestations of the disease even the characteristic "snuffles." Within a few days of the birth of the infant it is observed that it cannot move its limbs. Not all of them may be involved however, it may be a leg or an arm, or the legs and not the arms, or the arms and not the legs. The affected limbs are motionless and any attempt to move them causes the infant to cry. There is swelling at the epiphyseal line, which, in a bone superficially situated (as the lower epiphysis of the humerus, radius or tibia), can easily be detected. If the upper epiphysis of the humerus is affected this swelling however may escape notice and if the child has been delivered with forceps or if the labor has been unduly delayed it may be confused with birth paralysis of the upper arm type. In some instances the swelling may involve the entire limb.

Most of these cases recover without any loss of function. In fact if properly diagnosed and treated recovery takes place in a remarkably short time. In cases which have not been diagnosed and treated the process may go on to suppuration and permanent separation of the epiphysis. The joint may become involved and osteomyelitis develop, and should the child survive the added pyogenic infection the function of the limb will be lost. This pseudo-paralysis of Wegner somewhat resembles scurvy but the fact that it appears at birth and not eight or nine months later will exclude this dyscrasia.

Congenital Tertiary Syphilis of Bones.—As in the tertiary stage of the acquired disease, congenital osseous syphilis later causes periostitis, osteitis and osteomyelitis. Before the third year the lesions usually take the form of periostitis, affecting in the majority of instances the long bones—the femur, the tibia and fibula and the bones of the arm and forearm. This periosteal inflammation is usually confined to the shaft but may involve the articular surface in which event arthritis develops, often accompanied with a considerable degree of hydrops. There is pain in the bones which become considerably thicker, especially on their anterior aspect due, as in the acquired disease, to a round cell infiltration of the periosteum. Unless absorbed by treatment this periosteal infiltration condenses and forms new bone which gives rise to thickenings and exostoses that persist for life. The bones of the skull, especially those forming the cranial vault and forehead, are also sometimes

affected, although less frequently than the long bones. The lesion here presents as a more or less circumscribed swelling, slightly red and tender to the touch, and it may be single or multiple. If not absorbed the eburnation that later occurs gives rise to the nodes or bosses sometimes observed on the skulls of congenital syphilitics. These exostoses are often very pronounced—so pronounced in fact that they remind one almost of horns. On the forehead, by increasing its height and width, the so-called "Olympian brow" is produced, which is so frequently seen in children and adults who have, or have had, congenital syphilis. When present on the vertex, these bosses frequently assume a cross-bun appearance which is striking and characteristic.

Osteitis and osteomyelitis, as in the acquired disease are late manifestations of congenital syphilis. Not infrequently these deeper and more destructive lesions are secondary to a primary gummatous periostitis. These lesions are essentially gummatous, but differ from the gummatous osteitis and osteomylitis occurring in the acquired disease in being of much slower development. The process begins with pain, which is worse at night. As a rule these congenital, osteocopic, pains are not severe and for that reason are sometimes mistaken for rheumatism or "growing pains," especially if the congenital syphilis is of that type in which cutaneous or nervous lesions are not present. Pyogenic or tuberculous infection may occur, and this further complicates the process in addition to making the clinical diagnosis more difficult. By reason of the slow development of these lesions there is never any symptoms of acute inflammation. Sinuses however, usually form and sooner or later there is discharged a sequestrum of bone, or there may be several of these before the process heals which it may do with considerable loss of structure.

While no bone is exempt, the long bones are most frequently affected, next in frequency are those of the skull. It is well to remember in this connection that tuberculosis rarely if ever attacks the bones of the cranium in childhood and therefore any osseous lesion of these bones in childhood when trauma can be ruled out is almost invariably syphilitic.

Dactylitis.—A form of osteomyelitis that occurs in congenital syphilis and, also much more rarely in the acquired disease, is dactylitis. It is by no means frequent—not nearly as much so as when due to tuberculosis—but it is one of the bone lesions of congenital syphilis that is more frequently confused with tuberculosis than any other. This is particularly true if the carpal and metacarpal bones are also involved. Usually but one phalanx is involved, but sometimes there may be several. The finger becomes red and swollen—so swollen in time that it assumes a distinct

fusiform appearance that is quite characteristic. This swelling comes on without much pain and is several months in reaching its maximum size. The gummatous process then has had time to reach the cutaneous surface and a sinus forms down to the diseased bone, which affords passage for sequestra. Unless checked by treatment the finger or fingers affected may be rendered almost useless by the destruction of the bone. Less frequently, the toes and foot are attacked in a similar manner.

In diagnosing from tuberculosis, as I have already inferred, the clinical signs are of comparatively slight value. In congenital syphilis there are probably signs of the disease elsewhere; then there is the Wassermann reaction. If the process is syphilitic it will clear up promptly under antisyphilitic treatment. If it is tuberculous it will not. If it is a mixed infection, *i. e.*, that is tuberculous and syphilitic combined, as is not infrequent, it will at least be benefited by antisyphilitic treatment.

CHAPTER XXXVIII.

SYPHILIS OF THE GENITO-URINARY TRACT.

Previous to Rayer who wrote in 1840, syphilis of the kidneys was not recognized. This is not difficult to understand when we realize the knowledge or rather lack of knowledge of pathology previous to the time of Virchow. For, while Salicete described "renal dropsy" in 1476, it was not until 1770 that Cotugno discovered albumin in the urine and ascribed it to nephritis.

Syphilis of Kidney.—Our knowledge of renal syphilis therefore, may be said to have begun with Rayer who wrote as follows: "It is not easy to appreciate thoroughly the influence which constitutional syphilis may exercise upon the development of albuminous nephritis; for it is very rarely that we see this latter disease in individuals affected with constitutional syphilis who have not been subjected to the action of other causes, the influence of which upon the development of the disease in the kidneys cannot be disputed. I have seen cases however, in which the influence of the venereal constitutional affection has appeared to me so striking that I have not hesitated to attribute the development of the disease in the kidneys to the venereal cachexia." Thus did the French physician first combat the generally accepted opinion, and one which is still held by many, that the nephritis sometimes occurring in early syphilis is due to the action of mercury alone. For, before the time of Rayer, the Englishmen, Wells, Blackall, and Gregory had observed nephritis in the early stage of syphilis, but had attributed it in every instance to the action of mercury upon the kidneys. In 1867, Guiol published a thesis on syphilitic albuminuria and in the same year Perroud presented a comprehensive description of acute syphilitic nephritis. The studies of Spiess and Wagner came later and in 1898 Karvonen critically reviewed the entire literature of syphilis of the kidneys in an exhaustive monograph which even now, after the lapse of nearly a quarter of a century which has brought forth the Treponema pallidum, the Wassermann reaction and arsphenamine is well worth the reader's study. Since then more has been learned, and it is my purpose in this chapter to set forth our present knowledge of syphilis as it affects the genito-urinary tract.

Nephritis in Secondary Syphilis.—Acute nephritis occurring in secondary syphilis usually comes on within the first six months of

the infection. It is frequently of serious import. Fournier asserted that one-third of such cases terminated fatally, but Karvonen found a larger percentage of recoveries as did also Rose Bradford who further observed that the condition was prone to become chronic or to show a remittent tendency with persistence of the albuminuria. It is these cases which undoubtedly later progress to amyloid change which is not infrequently observed in tertiary syphilis. Wright is of the opinion that nephritis occurring in secondary syphilis always connotes malignant syphilis, but with this I am not in accord. Secondary syphilitic nephritis in my opinion depends entirely upon the kidneys as a *pars minoris resistentiæ* which have been rendered so in many instances by chronic alcoholism and other enervating cachexias.

The nephritis that occurs in secondary syphilis due to the infection rather than to the nephrotoxic action of mercury or arsphenamine is of two types. In one, which is by far the most frequent and which is much more frequent than is usually supposed, it is mild and transitory. The amount of albumin present in the urine never exceeds 20 to 30 cm. to the liter and the urinary toxicity is low. While casts are present they are not numerous, and the ophthalmoscope may show no albuminuric retinitis or only to a slight degree. Headache and backache may or may not be present. According to Dieulafoy and also to Mauriac this form of nephritis occurs much earlier than the second form. Not infrequently it is coincident with the chancre. It is undoubtedly due to an acute invasion of the kidneys by the Treponema pallidum—an ephemeral visceropathy as it were, such as occurs with considerable frequency in early secondary syphilis and which, under treatment, rapidly passes away leaving no trace. This form of albuminuria need cause no alarm and is not a contra-indication for arsphenamine, although as a matter of precaution it is wise in my opinion to refrain from giving mercury in these cases until the urine is entirely free from albumin.

The second type of syphilitic nephritis is that which is referred to by Fournier and, as I have already stated, is a serious condition. It occurs somewhat later than the first—usually after the sixth month of the infection. As a rule it is of insidious onset but the symptoms may be fulgurant from the beginning, which is of most unfavorable prognostic import. The patient complains of malaise and headache. There is also a slight rise of temperature. In some instances edema is the first symptom, which may be general or localized in the eyelids, genitals or lower extremities. Backache is usually complained of but fever is often absent. When it is present it is usually accompanied by gastric disturbance such as nausea and vomiting. During this time and even when the edema has come on, the amount of urine passed may not be appreciably

diminished; but in a very short time—a few days at most—it diminishes very much in amount and the albumin content increases enormously. This albuminuria is best described by the adjective "massive" and it is characteristic—I may even say pathognomonic—of this form of syphilitic nephritis. An idea of its intensity may be conveyed when I say that the amount of albumin present varies from 10 to 60 gm. to the liter. The amount of urea is markedly decreased and the toxic elements which produce acidosis are markedly increased. Microscopic examination of the urine shows numerous red blood cells, renal epithelia and all kinds of casts.

Doubly Refractive Lipoids in Syphilitic Nephritis.—In 1914 Munk called attention to the presence of doubly refractive lipoids in the urine of syphilitic nephritis. These doubly refractive lipoids were only occasionally present in nephritis due to other causes and then not in abundance; but in the urine of syphilitic nephritis they occurred with much frequency and in abundance. Stengel and Austin also called attention to the frequent presence of these doubly refractive lipoids in the urine of syphilitic nephritis. I am in accord with Stokes that while not conclusive, the presence of these peculiar fat globules—for such they are—is strongly presumptive of syphilitic nephritis.

The permeability of the kidneys as shown by the time elimination test with methylene blue is not disturbed, or only slightly delayed. The action of the heart is not increased and there is no arterial hypertension. In all these cases acute uremic coma may suddenly develop and in it the patient may die. Sometimes the patient dies from acute edema of the glottis or of the lungs. Sometimes death occurs from progressive edema, the fluid invading the cavities of the thorax and abdomen. Recovery may gradually take place. I am not as pessimistic as Fournier in regard to the percentage of deaths. I do not believe that one-third of these patients die of this disease. Some do, it is true, but they are the exceptions. I do believe however, that many of these cases develop amyloid kidneys in after years and in some instances may succumb to this affection. This is borne out by the researches of Rosenstein who reported on 120 cases of renal amyloid disease. Of these 32 were due to an original syphilitic nephritis. Out of 265 cases of amyloid kidneys reported by Wagner, 36 could be traced to the same cause.

Treatment.—In the treatment of this form of nephritis we are confronted with two propositions as it were. Of these, one is that we are dealing with a specific infection that can only be conquered by specific drugs. The other is that both of these specific drugs—arsphenamine and mercury—when given in therapeutically effective doses, are more or less nephrotoxic in their action. This places us, to use an ancient vulgarism, "between the devil and the deep sea."

But here we can regard another ancient saw, "of two evils choose the less." Arsphenamine has a much less deleterious action on the kidneys than mercury, therefore arsphenamine should be used. It should be given in small doses, *e. g.*, 0.2 gm. every few days—the urine being frequently examined to note its effect. At the same time the edema should be overcome with freshly prepared infusion of digitalis —a tablespoonful t. i. d. Hot rectal irrigations of a gallon or more should be given daily. Hot packs or dry cups over the loins are also aids to the stimulation of the renal function. Diuretin, in doses of 0.6 gm. t. i. d. should be given. The patient should be kept on an exclusively milk diet. The intake of fluids should be carefully measured in comparison with the amount of urine passed, and while the edema is present should not be allowed to exceed it. Should uremia supervene phlebotomy must be done at once and the blood withdrawn replaced by a similar amount of a 2 per cent sodium bicarbonate solution, intravenously.

Kidney Lesions in Tertiary Syphilis.—In the tertiary stage disease of the kidneys manifests itself either as amyloid disease or as chronic interstitial nephritis. Amyloid degeneration is one of the early tertiary manifestations as it is nearly always a sequela of a secondary nephritis. It usually appears about four or five years after such an attack. Amyloid kidneys are invariably associated with amyloid changes in other organs, notably the liver, frequently the spleen and sometimes the intestinal glands. In amyloid kidney disease due to syphilis the symptoms are the same as when the condition is due to some other cause. There is the same anemia, the same waxy complexion and low arterial tension. Cardiac insufficiency is present and by reason of this general anasarca with invasion of the serous cavities of the thorax and abdomen may develop. Urinary examination shows the characteristic waxy casts and the two forms of albumin—serum and globulin. In regard to the prognosis of amyloid kidney disease due to syphilis I am in accord with Elsner that it offers a much better prognosis than when due to other causes such as tuberculosis or prolonged suppuration.

Chronic interstitial nephritis—sclerotic kidney, small red kidney —is usually attributed to alcohol. It is my opinion based upon considerable experience that it is just as frequently, if not more so, due to syphilis. It is essentially a tertiary lesion and is a remote sequela in many instances of a mild secondary nephritis. The symptomatology does not differ from the chronic Bright's disease due to other causes and its pathology precludes the possibility of a cure. However, I believe with Osler that a patient may live comfortably many years with chronic interstitial nephritis. To tell a patient that he has it does not necessarily mean the pronounce-

ment of a sentence of death in a short time. Gummata of the kidney can and do occur. As a rule they produce no symptoms or if they do they are vague and undefined. Most often their existence is discovered at necropsy.

Syphilis of the Bladder.—Syphilis of the bladder was first mentioned by Morgagni in 1741. Fifty years ago Lancereaux suggested its possibility but did not record any personal knowledge of its existence. In 1879 Proksch described six cases from the literature which comprised all that had been written up to that time. In 1909, by means of the cystoscope, Levy-Bing demonstrated that in the secondary stage of the disease there were definite erythematous patches similar to those appearing on the cutaneous surface. These patches may ulcerate and if situated in proximity to the neck of the bladder may cause tenesmus and increased frequency of micturition. There is no change in the urine, although as in all forms of vesical tenesmus a few drops of blood or bloody urine may be passed at the end of the urinary act. The condition is fleeting and soon passes away. It is only rarely encountered.

When tertiary syphilis attacks the bladder, which it sometimes does, although rarely, a different picture is presented. We now have to deal with the gumma and all that it implies. Gummata of the bladder are usually multiple, but they may be single. They are of insidious development and for a long time produce no symptoms, except perhaps, increased urination or some slight and vague vesical discomfort. If the patient is a man over fifty as frequently happens, or if there is a history of a long standing gonorrhea or if the patient has or has had a stricture, in many instances the physician looks no farther and assumes that the trouble of which the patient complains is due to the prostate or to a recrudescence of the gonorrheal infection. Sooner or later however, in nearly every instance the patient has a profuse hemorrhage from the bladder. Very frequently this is the first and only symptom of the condition. This hemorrhage is due to the gummatous process ulcerating through a vessel. It is not attended with pain and is not influenced by rest or posture and may continue intermittently for days. The bladder sometimes becomes so filled with clots that retention occurs. Appearing as it does in men approaching or past fifty years of age there may arise a suspicion of malignancy, or of a rupture of a vesical varix, or, if in a younger man, of tuberculosis, and in any event these causes must always be excluded. A cystoscopic examination should be made which will help somewhat in the diagnosis although it is my opinion that tertiary lesions of the bladder cannot be definitely determined by the cystoscope alone. The lesions are usually present in two forms. One resembles a papilloma—flat however, and not sessile. The other is frankly

gummatous in appearance—a punched out ulcer with a necrotic base and surrounded by engorged vessels and a red and angry looking mucosa. The necrotic base is sometimes detached in parts and floats free, revealing dark red nodules beneath projecting from the floor of the ulcer, of which there may be several. These growths are strongly suggestive of carcinoma, especially if they have existed for a long time and the bladder wall is much thickened by the consequent infiltration. In such cases the therapeutic test is the best method of differential diagnosis. In carcinoma syphilis may also be present and therefore give a positive Wassermann reaction; but if the lesion is purely syphilitic it will surely and promptly respond to antisyphilitic treatment, whereas if it is carcinoma, even if grafted upon syphilis, it will not. The absence of tubercle bacilli in the urine, or from a scraping of an ulcer made through an operating cystoscope, the shallower depth of the ulcers and the fact that they appear at a later age than in tuberculosis, and that they are attended with much less pain, and that they are unfavorably influenced by injections of silver nitrate as invariably happens when the ulcers are tuberculous, are factors to be considered in making the diagnosis aside from the Wassermann reaction.

Bladder Involvement in Syphilis of the Nervous System.—In syphilis of the nervous system, especially tabes dorsalis the bladder is often involved. Slowness of urination and inability to completely empty the bladder are often the first symptoms to be noticed in involvement of the cord. In tabes insensibility of the bladder is frequently present. The viscus may be enormously distended with urine and the patient may be totally oblivious of the fact. Atony of the bladder wall and paralysis of the sphincter which allows the urine to continuously dribble are frequently present and with other signs may be regarded as pathognomonic of degenerative changes in the cerebrospinal axis. Should cystitis develop in the course of tabes the inflammation causes a thickening and trabeculation of the bladder wall. This inflammation may extend upward through the ureters and cause a pyelonephritis. The absorption of toxic urinary products in these cases produces a low fever which is characteristic in tabetics with involvement of the bladder. When examined cystoscopically the internal sphincter vesicæ is found to be much relaxed, so that the instrument can be introduced with much less pain than is ordinarily experienced. This painlessness upon cystoscopic examination may be said to be pathognomonic of the tabetic bladder.

Syphilitic Involvement of the Prostate.—In the secondary stage of syphilis the prostate and seminal vesicles are not affected. In the tertiary stage in rare instances they are. Thompson has gathered an imposing array of cases from the literature but of

these I am inclined in many instances to doubt the correctness of the diagnosis. It is undoubtedly true, however, that in rare instances gumma of the prostate does occur. Because of the rarity of the condition it is difficult to describe the symptoms. Since gummata are usually painless it can be presumed that pain is not a prominent symptom; also, since a gumma is a neoplasm, more or less irregular enlargement of the prostate is to be supposed. The direction this enlargement takes necessarily determines whether residual urine with its concomitant symptoms is present or not. Gummata of the prostate lack the stony hardness felt in tuberculosis of the gland. Neither is the surface of gland as revealed by rectal examination, studded with the small nodules characteristic of tuberculosis. The age incidence of syphilitic disease is also much later, although not so late as in simple hypertrophy—it is met with in late middle age but not in senescence. Gumma of the prostate does not necessarily involve the bladder, whereas in tuberculosis of the prostate the bladder is in almost every instance involved. Prostatic gummata are nearly always multiple and can be felt as soft tumors in the substance of the gland. These soft tumors are characteristic and when felt should always arouse a suspicion of syphilis. A positive Wassermann reaction and the fact that gummata resolve under treatment are in most instances sufficient to make a diagnosis.

Syphilitic Involvement of the Seminal Vesicles.—There is no record of syphilitic involvement of the seminal vesicles There is no reason to doubt however, that such involvement can and does sometimes occur. Syphilis of the prostate and of the seminal vesicles offers a fertile field for research and one which will undoubtedly some time yield many facts now only surmised. I am becoming more and more convinced that senile prostatic hypertrophy is sometimes remotely due to a diffuse or circumscribed gummatous process that has proceeded to fibrosis.

Syphilitic Involvement of the Urethra.—Long ago Lancereaux stated that the analogy of structure between the urethra and the larynx would indicate that the lesions which affect these remotely removed parts would be identical. His contemporary, Virchow also recognized this when he said: "The ulcerations and cicatrices of the canal of the urethra are very well known; they have exactly the same characteristics as those of the larynx." In spite of this, secondary and even tertiary lesions of the urethra are much less frequent than of the larynx. In the secondary stage McDonagh states that a urethritis sometimes occurs that closely resembles gonorrhea. I do not question this statement but I am convinced that it is of extraordinary rarity. Chancre of the urethra sometimes occurs and when it does it may give rise to a slight discharge but this discharge can never, by any stretch of the imagination, be

mistaken for that caused by the gonococcus. On the whole the urethra is comparatively exempt in syphilis except as to the rather infrequent chancre of the urethra.

Syphilitic Involvement of the Penis.—What has been just said about the urethra also applies to the penis. While it is of course the most frequent site for the chancre the penis nearly always escapes from the later manifestations of the disease. In the eruptive stage however, a macular or papular eruption may be present here as elsewhere. If the foreskin is long, most papules are frequently observed on its inner lining. Mucous patches are also sometimes seen at the peno-scrotal angle. *Chancre redux* or relapsing chancre which is nothing more than a gummatous lesion occurring, sometimes after many years, on the site of the original sore is met with comparative frequency. Since I have discussed it at length in the chapter on the Chancre I will make no further mention of it here. The most characteristic lesion of the tertiary stage however, which affects the penis, is the infiltration of the corpora cavernosa and their fibrous sheath—Buck's fascia—and the subsequent condensation of the same into plaques or flattened nodules of almost stony hardness, which frequently leads to distortion of the penis and consequent inability for coitus. These indurations are sometimes observed in gout and diabetes. They may also occur in the course of an old gonorrhea but in this condition the corpora cavernosa are less apt to be involved than the corpus spongiosum, usually at the bulb; these cases resemble stricture of the urethra.

When this condition presents itself to the patient, who usually discovers it by accident, it frequently causes him much concern and he forthwith consults a physician. It has been my experience that anything which affects the penis is always a matter of grave moment to the layman. Ricord has graphically described this condition and I can do no better than to give his description. "Sometimes," writes the great Frenchman, "in a patient in the third period of syphilis, it happens that a small, hard point shows itself in one or both of the corpora cavernosa. Some day, without having been warned by any pain, by any appreciable phenomena, the patient feels in the substance of the penis, a small induration of the size of a millet seed. By degrees this induration increases in size, advancing sometimes on one side only, sometimes on both, not occupying any one point of the corpora cavernosa in preference to others; thus, it is met with as frequently above or below or laterally. The disease progresses slowly without any pain; but in proportion as the induration extends, causes the penis to deviate from the straight line, and the result is that, if the induration be situated laterally in one corpus cavernosum only, the erectile tissue loses its permeability at the point indurated; when the patient has an erection, the

corpus cavernosum of the sound side only becomes distended, that of the diseased side retaining the dimensions of the flaccid state, and the penis describes a curved line with a lateral concavity; the patient has an erection which might be called inguino-crural, the extremity of the penis being directed toward the fold of the groin. If the seat of the induration is the dorsum of the penis, the latter is curved upward and backward, the glans being brought in proximity with the symphysis pubis."

These indurations are not influenced by treatment with constitutional remedies. The giving of iodides as recommended by some is in my opinion useless. The best that can be affected by the specific drugs is to prevent other nodules from forming. In some instances their surgical removal may be indicated.

Syphilis of the Testicle.—Syphilis of the testicle is comparatively frequent. With the possible exception of the kidneys it is the most frequent lesion of the genito-urinary apparatus. It is essentially a tertiary manifestation although it sometimes happens that acute orchitis or epididymitis or both may present in the secondary stage. Such an event is however, very rare and for descriptive purposes may be disregarded. When tertiary syphilis attacks the testicle there is nearly always to be found a similar gummatous lesion elsewhere. For that reason it has been assumed by some that gummatous disease of the testicle connotes a severe tertiary stage. With this I am not in accord except in so far as a tertiary lesion is always indicative of a more or less active state of the disease.

When syphilis attacks the testicle it usually does so as an orchitis —the epididymis becoming involved later. In passing I would say that this is just the opposite of what occurs in tuberculosis in which the process usually begins in the epididymis. The condition may be bilateral or unilateral, usually it is unilateral. It occurs either as a diffuse gummatous infiltration which later becomes fibrous or as a circumscribed gumma which may ulcerate and form a projecting fungoid mass, the so-called fungus testicle. I wish to say, however, that not every gumma of the testicle takes this formation, which, in my opinion, has been more written about than seen. More frequently it appears as an excavated ulcer with no tendency whatsoever to form exuberant granulations.

Gummatous infiltration is the type most frequently encountered. It occurs as a slow enlargement of one or both testicles—the epididymis being for a considerable time not involved. It is painless and the only discomfort it may cause is the feeling of weight and dragging on the cord which is often what first attracts the patient to the condition. As the process becomes more pronounced and involves the tunics of the testicle there is frequently present a slight hydrocele. The epididymis also becomes involved in whole or in

part—the globus major usually becoming affected first, whereas in gonorrhea the globus minor is usually affected first. Sexual power may or may not be reduced; frequently it is not. Later, when the infiltrative process has undergone fibrosis, the testicle affected—in some instances it is both—can be felt only as a small fibrous mass imbedded in the scrotum. Should this be allowed to occur—and I wish to say here that if properly diagnosed it should not—the testicle is useless, and if both are affected complete impotence, with absolutely no hope of recovery, is the result.

Gumma of the testicle is usually single and as a rule unilateral. It begins as a small soft tumor, not unlike a small cyst when felt between the fingers. If there are more than one they usually coalesce to form a single large one, which, unless dissipated by treatment sooner or later breaks down to form sinuses leading down to the testicle or a crater-like ulcer or a fungous mass. In gumma of the testicle the cord is nearly always infiltrated as well although isolated gumma of the cord is extremely rare. Strange to say however, even in extensive gummatous lesions the vas deferens is only very rarely involved. So rare is this involvement that it has been suggested by Barr as possessing a certain diagnostic value in differentiating between tuberculosis and malignancy with which gumma of the testicle is most likely to be confused.

This differentiation between syphilis, tuberculosis and malignancy is sometimes extremely difficult. The syphilitic testicle is smooth and the enlargement is symmetrical. Quite frequently the epididymis is not involved. If it is, this involvement is late in appearing and the globus major is affected first. Pain is absent. In fact, the testicle may be abnormally insensitive as evidenced when pressure is exerted. In tuberculosis the epididymis is almost invariably involved first and as such can be felt as a hard nodular mass—the process almost invariably beginning in the globus minor. The testicle itself, while enlarged is studded with nodules which impart to the palpating fingers a peculiar uneven surface which is not present in syphilis. Pain is always a predominating feature and in tuberculosis sooner or later sinuses form which lead down to the epididymis. In diffuse gummatous infiltration these sinuses do not form—they only form with gumma. Also, the sinuses which form with gummata never lead down to the epididymis but to the testicle itself. Once the condition reaches its maximum it remains stationary if syphilitic and then gradually shrinks as the cellular infiltration becomes transformed into fibrous tissue. In tuberculosis, sinus formation takes place long before this shrinkage occurs. In the active phase syphilis of the testicle responds rapidly to constitutional treatment. Arsphenamine and mercury have no effect upon the tuberculous testis. If the testicular lesion is tuberculous

it is nearly always attended with evidences of tuberculosis elsewhere. It may be the prostate or bladder or both, the kidneys, the intestines, or lungs. In other words there is nearly always evidence of a generalized infection—miliary tuberculosis or phthisis pulmonalis. Acute gonorrheal epididymitis is as a rule not difficult to diagnose although it may sometimes be confused with acute syphilitic epididymitis occurring in the secondary stage. The presence of active secondary lesions elsewhere or only recently absent, and the positive Wassermann reaction, usually enable the diagnosis to be made if the lesion is syphilitic. This is still further confirmed if there is no gonorrheal history, but if the history is complicated with a recent gonorrhea it may be necessary to resort to the therapeutic test.

Malignant Disease of the Testicle.—Malignant disease of the testicle is sometimes extremely difficult to diagnose from syphilis. Nor does the Wassermann reaction always clarify the diagnosis. For it must be remembered that with malignant disease as with tuberculosis, syphilis is sometimes present. There are certain clinical facts however, which in many instances enable a correct diagnosis to be made aside from the therapeutic test which should invariably be resorted to where there is any doubt. In malignant disease the growth is always much more rapid than in syphilis. If the growth be what is known as a "colloid cancer" its rapidity of development is such that there is never any question as to what it is. The inguinal glands are always involved in malignancy, which they are not in syphilis. Cachexia is sooner or later present in malignancy, whereas in syphilis the patient may enjoy comparatively good health. To my mind, the most important diagnostic feature in malignancy observable to the naked eye is the presence of tortuous veins on the distended scrotal integument. These are never present in syphilis.

Syphilis and Sterility.—Syphilis undoubtedly causes sterility. As long ago as 1861, Lewin observed in the semen of syphilitics in which no other abnormalities could be discerned that only 50 per cent contained active spermatozoa. That azoöspermia can be caused by syphilis which is otherwise asymptomatic has been noted also by Casper, Taylor, and others. In these cases however, I am convinced that there is some lesion of the generative apparatus that may be silent in so far as symptoms are concerned but which nevertheless is the cause of the condition. Syphilis *per se*, cannot, as some have imagined, cause sterility either in the male or female; but it can and undoubtedly does give rise to some local process which produces it.

The Urine.—The Treponema pallidum has been found in the urine in active secondary syphilis. Such findings however, are rare and offer many difficulties; they are of no practical importance.

Complement-fixation tests with urine have been done but they are exceedingly liable to produce falsely positive results owing to the highly anticomplementary activity of the urine. For this very obvious reason a Wassermann test of the urine possesses absolutely no diagnostic value.

Renal Lesions in Congenital Syphilis.—In congenital syphilis the renal lesions are apt to be those of defective development rather than inflammatory. Syphilitic renal disease undoubtedly occurs *in utero* as is evidenced at necropsy of infants dying shortly after birth and from the examination of still-born fetuses. Canelli states that sclerotic atrophy, gumma and retention cysts of the kidneys have been observed in such.

Congenital syphilis undoubtedly causes parenchymatous nephritis; usually between the fourth and sixth year of life. This congenital syphilitic nephritis does not differ from that following the exanthemata and for that reason it frequently is ascribed to some cause other than syphilis. It is of grave prognosis unless the cause can be ascertained. It is sometimes, as in adults, followed by interstitial nephritis, which is hardly if ever observed in infancy; it may be followed as in adults by amyloid disease.

Infants with congenital syphilis are frequently attacked with diffuse gummatous orchitis. The testicle—one or both—usually both, is increased in size but painless. Unless treated constitutionally fibrosis ultimately sets in and the organ becomes reduced in size but painless. Gumma of the testicle in congenital syphilis is extremely rare.

Syphilis of the female organs of generation is discussed in the chapter on Syphilis and Gynecology and therefore will not be repeated here. As a rule syphilis only rarely attacks the kidneys in females and even more rarely does it attack the female bladder. The nephritis or cystitis arising therefrom does not differ from that occurring in the male.

CHAPTER XXXIX.

TERTIARY SYPHILIS OF THE EXTERNAL FEMALE GENITALS.

It is usually supposed that tertiary syphilis of the external female genitals is of very rare occurrence, although the frequency of secondary lesions is readily conceded. The reason for this is that it is by no means easy to find clinical material with which to illustrate the tertiary stage of the disease in this particular region. The usual account to be found in text-books and in didactic teachings is that lesions in this locality are very rare and when they do occur do not differ much from similar lesions situated elsewhere on the body—such as gummatous nodules and ulcers.

The lesions of late syphilis occurring on the vulva or the vulvo-anal region closely resemble the so-called ésthiomène of the older writers. So close is this resemblance that what was formerly supposed to represent a separate pathologic entity is now believed to be nothing more than a manifestation of syphilis. Purely syphilitic lesions of the vulva of this type were described at length by the late Robert W. Taylor in 1907. Taylor had been investigating the subject for nearly twenty years and his knowledge and insight pertaining thereto were unequaled. He regarded this—as called by him—indurative edema of the vulva as a lesion which could occur either early or late in the disease. The early type he looked upon as a complication or sequela of chancre; the later he believed could occur without the history of a primary lesion. In this connection it must be stated, however, that he wrote before the Wassermann reaction came into use. The lesions were seen by Taylor to develop after secondary condylomata, as I have also seen. A chancre or condyloma may persist for a long time. Each may even disappear and later recur, but what I shall discuss here are those cases which appear as tertiary manifestations.

Ésthiomène.—Taylor's idea of a late lesion is one which appears about three years (seldom later) after infection—a time really when the tertiary stage can hardly be said to have begun. Nor can it be said that he regarded these lesions as the same or in all respects similar to ésthiomène, which term signifies a lupus or corroding process. But as I understand ésthiomène, and the same is true of others who have written on the subject, the ulceration is only

secondary and accidental, as it were: it is a proliferative process pure and simple. Very seldom was a true ésthiomène considered as a part of syphilis and as I have already stated was not associated with the disease until the advent of the Wassermann reaction. As was known to Taylor, it not infrequently occurs without any collateral evidence of an already existing syphilis. He believed it to be due to irritation of some kind or to trauma. The lesions which Taylor studied were identical, in part at least, with elephantiasis and it is known, and I can also recall an example, that elephantiasis is sometimes a complication of ésthiomène. The lesions described by Taylor certainly have a better prognosis than ésthiomène *per se;* they were not only benefited by specific treatment but by surgical

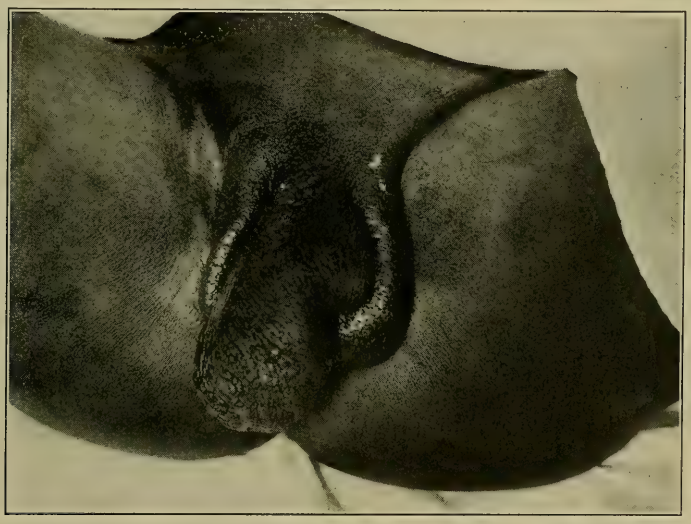


Fig. 69.—Syphiloma of vulva. (Courtesy of Dr. M. B. Parounagian.)

treatment as well. In Taylor's classic contribution the numerous illustrations show that the perineal and anal regions were involved as in ésthiomène. The phagedena which according to Taylor may complicate such cases in elderly women agrees well with the description of some cases of ésthiomène. But in my opinion these cases so involved represent a more acute process than does ordinary ésthiomène. Both tend to cause death, but both sometimes heal leaving great cicatricial deformity.

Taylor describes a case of a woman, aged twenty-five years, who had syphilis for three years and with secondary lesions still present. She gave a history of having been kicked in the vulva six months before, after which the nymphæ began to swell slowly and turn

purplish. The labia majora were also enlarged, the left more than the right which was of cartilaginous hardness. The inner surface of the parts showed marked lobulation and papillary hypertrophy. Unfortunately he does not follow up the history of this case further. He also describes another case of a negress, aged thirty years, who had syphilis four years. Here the labia majora began to swell, also unequally, the left more than the right so that it suggested elephantiasis. The integument was covered with small warty and papillomatous excrescences. The larger labium was excised and a portion of the tissue when examined under the microscope showed an indurative edema. In another case the patient was fifty years of age and no history of syphilis is mentioned. It is of course to be understood that no Wassermann was taken. She had a chronic indurative edema and for five years past an obliterative atrophy had been slowly taking place which also involved the perianal region. The sclerotic process was deep and the deformity marked. The distortion of the entire vulvo-anal region is described as "chaotic." No ulceration had occurred at any time. He does not state whether stricture of the rectum was present or not, although from the description he gives I infer it was. This case closely resembles the usual non-ulcerative type of ésthiomène. Taylor goes on to state that in uncleanly and dissipated women with profuse vaginal discharges ulceration may develop, either superficial or deep and burrowing. Sinuses may develop which may perforate into any of the adjoining cavities forming fistulous tracts not only of these but of the buttocks and thighs. Phagedena and gangrene may be superimposed upon a condition already sufficiently gruesome. In his latest paper Taylor does not allude at all to ésthiomène, which to me is passing strange, although in his bibliography he alludes to at least one article on the subject. Nevertheless recent authorities have included Taylor's contributions in the literature of ésthiomène and it is only just to say that he has done much to bring forward the syphilitic theory of the latter. His cases seem to form a connecting link, as it were, between obscure syphilitic lesions of the external female genitals and ésthiomène, for it must be admitted that clinicians of the past found nothing in common in syphilis and ésthiomène until the advent of the Wassermann. An exception to those who held this view must be made, however, in the great English syphilologist, Jonathan Hutchinson, who believed fully in the syphilitic nature of ésthiomène, and with whom I am in full accord.

Huguier's Types of Ésthiomène.—The history of the literature of ésthiomène since its first description by Huguier in 1849 is so complicated and misleading that I shall refrain from discussing it. Huguier included three types—a superficial serpiginous ulceration,

a perforating and a hypertrophic type. Not infrequently strictly tuberculous processes have been confused with ésthiomène due to the fact that tuberculous ulceration of the female genitals is often accompanied by hypertrophy of the parts. Clinically the two conditions are sometimes so much alike that the diagnosis can only be made by biopsy or the serological test. In a certain number of cases tuberculosis undoubtedly complicates ésthiomène. Of the 6 cases analyzed by Kurz 3 were certainly and 3 probably, syphilitic. Upon admission 3 were at once pronounced syphilitic (in 1 tuberculosis was an alternative diagnosis), 2 as ésthiomène and the sixth as vulvitis. Five showed marked hypertrophy of the vulva, all 6 showed ulceration of some kind, 1 had atresia of the vagina, 1 had stricture of the rectum, and 2 vulvo-rectal fistulæ. Kurz concludes her account by quoting Taylor's cases as typical examples of Huguier's ésthiomène. To quote other authorities, Veit inclines to the syphilitic theory, while Pozzi holds to tuberculosis. To understand these seeming discrepancies in the opinions of able men it should be remembered that one observer seldom sees more than a very few cases.

Older writers have commented upon the health and vigor of the patients in contrast with the severity of the local condition, but in the cases seen by Kurz not one was in good general health. In all but one woman the affection was comparatively recent—two or three years. In the one exception the disease was of eleven years standing and the process seemed to have extended into the peritoneum. Death occurred from cachexia although peritonitis had existed for a long time.

Affection of the Vulva.—Before proceeding further it may not be out of place to discuss briefly the pathology of vulvar affections. Although perhaps not so widely known as it should be, aside from that caused by gonorrheal infection it cannot be said that there is such a pathologic entity as chronic vulvitis. From analogy it is reasonable to expect to find chronic processes terminating in hyperplasia or atrophy; the first named possibly going on to sclerosis and the consequent shrinking which we call atrophy. We know that the vulva is more or less predisposed to lymphatic stasis and as a result of this tendency an elephantiasic hypertrophy may be present to a marked degree, but this does not necessarily mean that it is of inflammatory origin. In reality the two conditions are quite distinct, although it is conceivable that they may closely resemble each other or even coexist in a given case.

Elephantiasis and Ésthiomène.—An inflammatory hyperplasia of a high degree may simulate an elephantiasis but by the aid of the microscope we should find differentiation easy. Now, the findings in the hyperplastic tissue of ésthiomène are inflammatory with the

development of fibrosis—a type of inflammation which we know to be very common in syphilis. In elephantiasis there are no such inflammatory changes; only the lymphatics show hypertrophy. As far as known elephantiasic tissue never undergoes atrophic change, while in a purely chronic inflammation a tendency to regression in some form is almost inevitable. These facts in my mind are important in so far as they enable us to distinguish between a syphilitic condition as ésthiomène and elephantiasis.

In ésthiomène the area of hyperplastic inflammation includes the perianal region. But to state that a chronic productive inflammation followed by regressive changes in this locality can occur only in a syphilitic condition may be going too far. Certain tuberculous cases may present the same appearance microscopically. It has even been suggested that in some of these cases, the tertiary syphilitic lesions have been inoculated secondarily with tuberculosis. The possibility of this hybrid state of infection is a very real one in my opinion. Beyond question, constant irritation from neglect and filth, acrid discharges and other factors perhaps may combine to produce a simple inflammation. Upon examination of some of the cases on record this would seem to be a fact. In addition to these factors there is also the tendency of the vulva to suffer from lymph stasis and to this may be added the possibility of a stasis of the venous system. In this connection I would call the reader's attention to the very dependent position of the vulvo-anal region which in this regard resembles that of the legs and feet. In varicose ulcers it is well known that this dependent position is responsible for the chronicity of this condition and its marked tendency to relapse. It is not unlikely, therefore, that in the vulva the same inherent tendency also exists and thus explains in a measure the frequent recurrence of ulceration after partial or total cicatrization.

Tertiary lesions—ulcers and gummata—are rarely encountered in the external female genitals, but when seen they in no wise differ from the same lesions elsewhere. It has been stated that syphilitic lesions in this locality are relatively small and circumscribed. With this I am not prepared to agree. In regard to sclerotic tissue the result of a long-continued low grade inflammation, differences of degree undoubtedly exist. Kurz after an exhaustive study of six personal cases, has reached the conclusion that ésthiomène from first to last is indicative of syphilis. This view was also held by some older clinicians as well as by Taylor, Hirst and Veit. Other causative factors are filth, and the consequent irritation engendered thereby, and dissipation. This is exemplified by the fact that the majority of women afflicted were prostitutes of the lowest class.

There is no longer any doubt about confounding tuberculosis with ésthiomène although this diagnosis cannot always be made by

histologic examination alone, as giant cells and other concomitant elements of tuberculous tissue have been found in syphilitic tissue as well. As very properly emphasized by Kurz the fibrotic process caused by syphilis, and which so closely parallels simple inflammation, is not inherently different from gumma, although it never ends in softening and ulceration but, instead, in sclerotic change and deformity. She raises the point, which in my opinion is well taken, that the ulceration in some cases may have resulted from the breaking down of true gummata. The examination of the lesions in her personal cases was strongly suggestive of this probability. She would explain all the active phenomena of the disease, such as the ulceration and fistula formation, the strictures of the vagina and rectum, the involvement of the deep tissues such as the peritoneum, in this manner.

In order to decide this intricate problem, my advice is to rely upon the Wassermann. One test is not sufficient in a suspected case; it should be done repeatedly. If still in doubt, a provocative arsphenamine should be given, and the Wassermann taken again as described in another chapter. The stigmata of syphilis should be diligently searched for, not only of acquired syphilis but of congenital syphilis also. The entire family history should be carefully inquired into. This includes the infant mortality and the number of abortions, miscarriages and still births in the strain.

In the literature of stricture of the rectum due to syphilis numerous cases will be found which began with or were accompanied with the symptoms of ésthiomène. The contraction and deformity is common to both.

Kraurosis Vulvæ.—Before concluding this chapter, I wish to revert to the theory that there is a general process that is responsible for this fibroplastic and sclerotic vulvitis. Unless such a condition is recognized it is impossible to explain it. Where the process is very superficial and without a hyperplastic stage we note the condition known as kraurosis vulvæ which, as is known, eventually terminates in sclerosis and atresia of the vagina. Amongst Taylor's material one case is mentioned in which the symptoms approximated those of kraurosis and patients with the latter have frequently given a history of syphilis, acquired or congenital. With the tendency to lymph stasis and venous stasis and open to all manner of mechanical insults such as arise from coitus, irritating discharges and neglect of hygiene, that these chronic proliferative processes are not more common than they are, is remarkable to say the least.

While it is almost invariably syphilitic, I think it is going too far not to exclude non-syphilitic cases. They undoubtedly occur. The infrequency of the affection is in my opinion the reason why it is not better understood.

Treatment.—The treatment of these cases is on the whole extremely unsatisfactory. They do not respond to either arsphenamine, mercury or potassium iodide. If an active gummatous process is present this of course can be promptly checked; but as most of these cases when seen are far advanced in sclerotic changes antisyphilitic remedies are of no avail because the damage has been already done. The reason for this is not far to find although unfortunately it is not as well known as it should be. Arsphenamine and mercury destroy the cause, *i. e.*, the Treponema pallidum, but they have no influence on the tissues as such. These, after the removal of the cause, which in this instance is the organism mentioned, will resolve again to health if not destroyed. But where they are destroyed or rather transformed into a tissue of a lower plane such as scar or fibrous tissue, they cannot be brought back to life again. For this reason also potassium iodide, our most potent alternative, is of no avail. Potassium iodide acts only on cells of new formation causing them to resolve. On sclerotic tissue it is without effect. The administration of this drug in those cases where the cell transformation is complete is a most fatuous procedure. Plastic surgery along with antisyphilitic treatment in those cases which are amenable thereto, perhaps offers the only hope.

CHAPTER XL.

SYPHILIS OF THE GASTRO-INTESTINAL TRACT.

In spite of the fact that the buccal cavity and the pharynx and the anal orifice and the parts immediately contiguous thereto are frequently attacked by syphilis both in the secondary and tertiary stages of the disease, yet syphilis of the gastro-intestinal tract as compared with the skin, the bones and the nervous system is comparatively infrequent. That is, I would say, in so far as clinical confirmation is concerned. For, the researches of Warthin have conclusively proved that in syphilis there is a spirochetosis of all the viscera, which can by no means exclude the gastro-intestinal tract; a fact that goes far in convincing me that syphilis of the digestive apparatus is more frequent than is usually supposed.

Syphilis of Esophagus.—Syphilitic disease of the esophagus was mentioned by Severinus three hundred years ago. More than one hundred years later it was observed and described by Anstruc, by Ruysch and by Haller. In 1815, Carmichael discussed it in "An Essay on Venereal Diseases." Virchow described syphilitic lesions of the esophagus with considerable detail, but it was not until James West wrote his monograph in 1860 that this particular manifestation of syphilis received the attention it deserved. Since then Lublinski wrote an excellent thesis in 1883, and in 1914 the subject was thoroughly reviewed by Wile.

According to Wile esophageal syphilis is more frequent in males than in females, although strange to say, in the cases reported by West in his pioneer work, this sex incidence is reversed—he reported more females than males. When we take into consideration that alcohol may be a possible factor in determining the condition I am inclined to agree with Wile. Also, of some significance perhaps in the study of the literature is the frequent mention of lesions of the mouth and throat in connection with esophageal syphilis. It would suggest that continuity might play a part; the primary lesions being probably those of the buccal cavity.

The pathology and symptomatology of syphilitic esophagitis depends upon the stage of the disease when it occurs. Secondary lesions are rarely observed; the principal reason for this being in my opinion the rarity with which such cases come to necropsy. There is no record so far as I am aware of any of the superficial

erosions which occur with such frequency in the pharynx and buccal cavity having been observed in the esophagus; but the dysphagia so often complained of in early secondary syphilis may well be due to the presence of mucous patches in the gullet as well as in the mouth. This condition when present invariably disappears under treatment and need not be further considered here. The esophagitis and the sequelæ arising therefrom which warrant the attention of the physician occur only in the tertiary stage of the disease.

As would be expected in this stage the esophagus is subject to gummatous infiltration or to single or multiple gummata. So, too, the gummatous deposits when later transformed into cicatrices (which may happen because they have been allowed to progress undiagnosed), may cause more or less stenosis of this part of the alimentary canal and also dilatation or a diverticulum below the point of stricture. Or, the caliber of the canal may become so constricted that swallowing is impossible and the patient may die from starvation unless relieved by a gastrostomy.

Gumma or gummatous infiltration may occur at any part of the length of the esophagus but is usually encountered at or near the buccal or cardiac ends of the tube. Gummatous infiltration may be annular, completely surrounding the esophagus or only partly so; the long axis of the deposit is in the long axis of the esophagus. The infiltration usually begins in the submucous tissue but it may extend externally and become periesophageal. Gummatous infiltration rarely goes on to ulceration and for that reason pain may not be present. Owing to the swelling coincident with the process the patient may experience only some slight difficulty in deglutition which however does not improve but rather increases as the cellular infiltrate condenses and contracts by fibrosis. This is best defined by saying that at first there is no difficulty whatsoever in swallowing liquids and only slight difficulty in swallowing solid food. Later solid food can only be swallowed in small, well masticated bits; finally such food cannot be swallowed at all and liquids only with difficulty, or not at all. If the lesion is a single gumma or if there are several gummata more or less remote from each other, ulceration usually takes place and deglutition becomes more or less painful, although I wish to state that, as frequently happens in gumma elsewhere, pain may never be a prominent symptom. In this circumscribed gummatous type interference with deglutition may not be as marked as when the infiltration is diffuse. The subsequent cicatrix also may not interfere with deglutition, or only slightly so; the degree of stenosis being dependent upon the size and situation of the gumma.

Tertiary syphilis of the esophagus is to be differentiated from chronic esophagitis due to alcoholism or excessive smoking. The

symptoms of these conditions in no way differ from those due to syphilis before stenosis has taken place. Leukoplakia of the esophagus causes slight difficulty in deglutition and burning sensations as the food passes down. Like its congener, leukoplakia lingualis it is in the majority of instances of syphilitic origin. Following acute infectious diseases such as typhoid fever, diphtheria, smallpox and sepsis, esophagitis sometimes occurs; and when the condition resolves there may be more or less narrowing of the lumen of the tube. Benign growths may cause stricture of the esophagus but these are so rare that they may be well classed as pathologic curiosities. Aside from syphilis and carcinoma the most frequent cause of esophageal stenosis is that caused by drinking some corrosive liquid either with suicidal intent or by mistake.

Syphilis of the Esophagus Differentiated from Carcinoma.—The differential diagnosis between syphilitic disease and carcinoma of the esophagus is often extremely difficult. This difficulty is still further enhanced by the fact that carcinoma is frequently grafted upon an old syphilitic process so that the presence of a positive Wassermann reaction does not always give the necessary diagnostic help. The roentgen ray also affords little or no assistance. In many instances resort must be had to the esophagoscope and biopsy of a piece of the suspected growth. If the growth is high up it can sometimes be palpated externally; and when such is the case it usually indicates malignancy, as syphilitic growths are rarely large enough for this to be done. If the growth is small or if it is periesophageal there may be no obstruction to the passage of an esophageal sound which still further complicates the diagnosis. It is here that the esophagoscope can be used to advantage. In the early stages of carcinoma as in syphilis the mucosa may show no change; later also differential diagnosis may still be difficult because in diffuse gummatous infiltration, as in carcinoma, the mucous membrane loses its mobility and does not fall in folds as the esophagoscope is pushed downward. In both conditions the walls of the esophagus are rigid and the mucous membrane appears stretched and white and its surface dotted with minute hemorrhages. Ulcerated gummata are likewise difficult of diagnosis from carcinoma. Crater-like ulcers occur in both conditions and both are apt to bleed easily when touched with an applicator. Should, however, the growth appear like a cauliflower or a papilloma, syphilis can be excluded because the disease never manifests itself as such. Pain is more prominent in carcinoma than in syphilis and this element of pain should receive much consideration in diagnosis. In syphilis pain if present is felt only during the act of deglutition; in carcinoma the pain is continuous and is not confined to the esophagus alone but radiates toward the shoulder and the back of the neck. In

carcinoma paralysis of the recurrent laryngeal nerve is frequently present and may occur before any other symptoms. Along with this there may be involvement of the sympathetic nerve causing pupillary contraction and sluggish reaction to light. These symptoms, especially if occurring before dysphagia, would at once suggest syphilis of the central nervous system. In the event of this latter condition a lumbar puncture should be made, which if negative as to the Wassermann reaction would exclude syphilis. Should the growth extend backward paraplegia may occur, also before dysphagia. This too should be determined if of syphilitic origin by means of a lumbar puncture.

Stenosis.—Syphilitic stenosis of the esophagus must also be distinguished from the stenosis caused by pressure. Not infrequently this stenosis is due to a process affecting some neighboring organ or part that is in itself syphilitic. Examples of this are gummatous infiltration of the thyroid gland, aortic aneurysm, gumma of the mediastinum, gummatous infiltration of the cricoid cartilage or vertebral enchondroses. Not all of these processes are necessarily syphilitic but it cannot be denied that syphilis can and does produce any one of them. In stenosis thus caused the esophageal sound passes readily enough, only somewhere along its route it encounters an obstacle which seems to project into the lumen of the tube as it were. If the mucous membrane of the tube is movable the chances are in favor of compression stenosis. Here the roentgen ray is a valuable aid in diagnosis.

As I have already stated a diverticulum may form which is always above the obstruction. This diverticulum may be small or of such size that when filled with food that has not passed into the stomach it may cause dyspnea and aphonia from pressure. The symptoms may not be marked if the sacculation is not large and consist of nausea, expectoration and an increased salivary flow. There may be a feeling of pressure when solid food is taken. Vomiting and regurgitation of undigested food occur.

In all forms of esophageal disease it is of paramount importance to exclude syphilis in every instance. To do this it must be remembered that a positive Wassermann reaction is not always an absolute criterion that the process is syphilitic. The clinical signs must also be considered and these must, above all be subjected to a thorough therapeutic test. There are those who will question this because of the time element involved. But is this wise? It only requires three injections of arsphenamine given on three successive days, and then a week to await results. It is better to be safe than to be sorry; for I am in accord with Wile that syphilis of the esophagus has not infrequently been mistake for carcinoma of the same, with results that were far from being happy.

It must also be remembered that if the process has gone on to stenosis the lumen of the tube cannot be restored by constitutional treatment. Arsphenamine, mercury or potassium iodide cannot change scar tissue back to normal. The difficulty is purely mechanical and can only be overcome by mechanical means. Such cases are for the surgeon not for the syphilologist.

Syphilis of Stomach.—Keyes is of the opinion that syphilis of the stomach is almost as rare as syphilis of the esophagus. This is also the opinion of White of Boston. With neither of them am I in accord; rather do I agree with Warthin and with Morgan that gastric syphilis is rare because it is unrecognized. Although it is generally considered a rare and therefore from a clinical standpoint an unimportant form of the disease, gastric syphilis has been known since 1834 when Andral gave a detailed account of two cases. Since then several hundred authentic cases have been reported in the literature and a study of the necropsies of Chiari and later of Stalper would show that 1.2 per cent of all syphilitics are affected with gastric syphilis. The newer conceptions of syphilitic visceral pathology of which Warthin, Wile and others are the exponents, unite in confirming this; so that the study of gastric syphilis is well worth the attention of the clinician.

The frequency of functional gastric disturbances in the early secondary stage of syphilis are well known. While it is possible in not a few instances that these gastric symptoms may be due to a spirochetosis of the gastric mucosa as Warthin has shown, yet, it is my opinion, that in the majority of instances they are caused rather by the general toxemia of the disease; just as we find anorexia and dyspepsia in phthisis pulmonalis without any gross tuberculous lesions of the gastric mucous membrane. Whether this vague and ill-defined dyspepsia which occurs so frequently in early syphilis is due to the actual presence of the Treponema pallidum or is the reflex result of the syphilitic cachexia, it soon disappears under treatment, or even when treatment is not given or at best has been very inadequate and in the vast majority of instances the patient is never troubled by it again. The same is true of the gastric disturbances concomitant with syphilitic icterus; with the disappearance of the jaundice the gastric symptoms also disappear and do not return. Practically, this is all that can be said of early secondary gastric syphilis. In the late secondary stage and extending into the tertiary in point of time many patients complain of symptoms pointing to a chronic gastric catarrh. There is nothing distinctive about these symptoms. The diagnosis of gastric syphilis cannot be made from any pathognomonic symptom, for there is none. The symptoms also vary as to severity. In some cases they are only slight, while in others the distress arising therefrom causes

the sufferer to consult a physician. In the event of this unless active lesions of the disease are present, syphilis as the cause is rarely thought of, and the patient frequently "suffers much of many physicians," before the true cause is diagnosed and the condition, with few exceptions, promptly cured. The exceptions are those cases, now happily becoming rarer each year, in which the powers of digestion have been permanently disturbed by mercury and iodide administered by mouth for long periods of time. It is my opinion that in not a few instances the cure rather than the disease is the cause of the patient's gastric distress. Therefore, any patient with marked gastric symptoms which do not respond to treatment that under ordinary circumstances should affect a cure, who, further, gives a history of having had a chancre within five years or who has a positive Wassermann reaction, should be suspected of having gastric syphilis. A therapeutic test will either confirm or deny this diagnosis.

Tertiary Syphilis of Stomach.—Tertiary syphilis of the stomach originates either as single or multiple gummata of the stomach wall or as a diffuse gummatous infiltration. The submucosa is primarily and principally invaded, the process later extending into the other layers. Gummatous gastric ulcers are usually multiple but not infrequently they occur alone. They may occur either on the greater or lesser curvature of the stomach but as a rule they are found most frequently either at the cardiac or pyloric orifices. These ulcers are round or oval in shape and may be superficial or deep enough at times to cause acute perforation and a consequent fulminant peritonitis, or they may perforate slowly and give rise to a perigastritis. They are always surrounded by a dense induration and the vessels in the immediate vicinity show an endarteritis or an endophlebitis. A gastric gumma may sometimes grow very large—so large in fact that it can be palpated through the abdominal wall. Should the ulcer erode a bloodvessel hematemesis may occur, which, if the vessel is sufficiently large may be so profuse as to terminate fatally. The symptoms of syphilitic gastric ulcer do not differ from those caused by an ulcer due to some other cause. *Achylia gastrica*, deficiency of the gastric juice, is more apt to be present if the ulcer is syphilitic than if it is not. Pain is usually present and, as often occurs in syphilis, it is frequently worse toward evening. Other symptoms are vomiting, gaseous eructations, and in fact, all of the array which complete the clinical picture of gastric ulcer arising from any other cause. While there are no pathognomonic symptoms, the evening pain, the more or less absence of the gastric ferments and, as asserted by Kohn of Chicago, a greater tendency to hemorrhage, are more often associated with syphilitic gastric ulcer than with any other.

The symptoms of diffuse gummatous infiltration differ somewhat from those of the circumscribed gummatous ulcer. The gastric distress and the same aberrancy of the stomach secretions occur in diffuse gummatous infiltration as they do in gummatous ulcer. Hemorrhage however rarely occurs, although occult blood is frequently found, probably in larger amount than in other gastric diseases, always of course excepting carcinoma. If the infiltration is extensive it can sometimes be palpated and as a rule can be detected by the roentgen ray. The symptoms of diffuse gummatous infiltration of the stomach are never typical of syphilis. They may simulate any form of gastric disease, not excluding carcinoma. Pain may or may not be present. There may be anorexia or bulimia. Excessive thirst may be present or a craving for abnormal food, such as food containing an excess of acid—sour food.

Tertiary syphilis of the stomach is a disease of middle life; occasionally it is found in old age. It is twice as frequent in men as in women. It has no pathognomonic symptoms and may parallel in its clinical display any gastric disturbance from a chronic mild dyspepsia to a desperate carcinomatosis.

Tertiary gastric syphilis may give rise to such a degree of malnutrition that death may result. This is rare however, but frequently it makes the patient's life miserable for many years. In time these ulcers and infiltrations heal, and the patient may thus find a measure of relief. They heal however, by cicatrization and if these scars are extensive or impinge upon the cardiac or pyloric orifices of the stomach as they are very apt to do, they may cause eccentric contraction or dilatation of the viscus with the attendant distressing sequelæ which these deformities connote.

Tertiary gastric syphilis aside from inveterate gastritis due to some other cause is to be distinguished from gastric carcinoma and gastric ulcer—the so-called peptic ulcer of varied origin.

Syphilis Differentiated from Carcinoma of Stomach.—A circumscribed gumma or a diffuse gummatous infiltration may reach such a size that by palpation or by the roentgen ray it may perfectly simulate a malignant growth. It must also be remembered however, that gastric carcinoma, the same as tertiary gastric syphilis may run its course and not be discovered until necropsy. But in contradistinction to syphilis this course is immeasurably more rapid in carcinoma. The characteristic cachexia is always present in carcinoma; cachexia may or may not be present in syphilis. If it is, it is never as profound as it is in carcinoma. In tertiary syphilis there is never any glandular enlargement; in carcinoma glandular enlargement is invariable—especially the supraclavicular glands. Pain may be present or absent in carcinoma, usually it is a prominent symptoms; it may be continuous or there may be exacerbations

after eating. The same is true of syphilis except that the pain of syphilis is apt to be less severe and not infrequently is aggravated in the evening. Vomiting occurs in carcinoma in about 90 per cent of all cases; it also occurs in syphilis, but somewhat less frequently. Hematemesis occurs with much frequency in carcinoma; it is perhaps more frequent in gastric gumma and almost entirely absent in diffuse gummatous infiltration. There is nearly always present free HCl in the vomitus of carcinoma; in syphilis it is nearly always absent. The presence of the Boas-Oppler bacillus, a non-motile bacillus shaped like a base ball bat is said by some to indicate carcinoma when found in the vomitus, but it is not always present. It is rarely if ever present in syphilis. Edema and ascites are nearly always present in carcinoma during the last stage. These do not occur in syphilis unless the liver is also involved.

It must be remembered always in these cases that syphilis may complicate the carcinomatosis. For that reason the Wassermann is not always indicative that the growth is syphilitic. The therapeutic test must be tried and if the growth diminishes in size under such treatment it is syphilitic and not carcinomatous. In all cases therefore where there is the least doubt a course of constitutional treatment should be given and the results carefully observed.

Syphilis and Gastric Ulcer.—Syphilis was formerly looked upon as a most important cause of gastric ulcer and undoubtedly it not infrequently gives rise to this condition. But it must not be forgotten that syphilis and peptic ulcer may, and frequently do, coexist, and still be independent of each other. Gastric ulcer supposed to be syphilitic should be subjected to the therapeutic test. If it is syphilitic the ulcer will invariably disappear and the symptoms caused by it will disappear with surprising promptness. If it is not syphilitic, antisyphilitic treatment will have no influence upon it. It is practically impossible to differentiate between syphilitic gastric ulcer and that occurring from some other cause. The absence of free HCl in the stomach contents and the increased hemorrhagic tendency would in a measure point to syphilis but a diagnosis should not be made by these signs alone.

Brugsch and Schneider have advanced the interesting hypothesis that in some instances where chronic and rebellious gastric symptoms occur in tertiary syphilis, in the absence of gummatous disease, they are due to an irritation of the spinal nerve roots, similar to that in tabes but not so extensive. In other words, it is an abortive tabes with gastric symptoms only. This is possible and, in some instances, I believe probable.

Syphilis of Intestines.—Acquired syphilis of the intestines is rarely diagnosed clinically, although in many instances evidence of healed gummata have been observed at postmortem. Hazen is

of the opinion that it is more frequent than gastric syphilis. This I doubt, but I am in accord with him that it is not infrequent in the congenital form of the disease. Gummatous ulceration of the upper intestine has been recorded by Gutman. His case was that of a woman of forty years who presented a clinical picture resembling typhoid fever, with diarrhea, fever and emaciation. At necropsy the small bowel from the jejunum down showed multiple gummatous ulcers. Howers has reported a similar case in a man of twenty-three years who gave a distinct syphilitic history. His symptoms included a persistent diarrhea with bloody stools and abdominal pain and distention which was invariably worse at night. He subsequently died of pneumonia and at necropsy circular constrictions were found in the bowel as the result of cicatrized gummatous ulcerations. Fournier, and also Hayem, reported similar cases of intestinal syphilis which closely simulated typhoid fever. I cannot personally recall having seen any such manifestations of the disease. There is no reason to doubt that they occur, although with extreme rarity.

It is my opinion that some cases of ulceration of the duodenum with bloody stools are of syphilitic origin. This condition is usually ascribed to tuberculosis but if there is any doubt the Wassermann test and the therapeutic test will resolve the diagnosis. In 1904, Gaucher of Paris, and later Boas of Copenhagen discussed syphilis as a factor in appendicitis. Neither of these two eminent observers were able to find any corroborative evidence that would connect syphilis as a predisposing cause to either chronic or acute inflammation of the appendix vermiformis. Syphilitic gummatous ulceration has been known to attack the lower bowel—the colon—and to produce dysenteric symptoms, sometimes in an acute form, that bear a close analogy to amœbic or bacillary dysentery.

If we consider the mouth as the beginning of the gastro-intestinal tract and the rectum as the end it is these two extremities of the tract which are most frequently attacked by syphilis, both in the secondary and tertiary stages. Of the gastro-intestinal tract proper, that is from the beginning of the esophagus at the upper border of the cricoid cartilage to the external sphincter ani, the rectum is the part most frequently attacked—so frequently I may say that a knowledge of this phase of syphilitic disease is absolutely essential.

Tertiary Syphilis of Rectum.—Tertiary syphilis of the rectum occurs either as single or multiple gummata or as a diffuse gummatous infiltration. It is more frequent in women than in men and is frequently accompanied with amyloid degeneration of the abdominal viscera. Gummata are more frequent than diffuse gummatous infiltration, and when they occur they almost invariably ulcerate.

Not infrequently a gumma may be present in the rectum unknown to the patient who does not complain until after symptoms of stenosis set in. Gummata develop in the submucous tissue and vary in size from a small nodule about the size of a dime to an ulcerated mass that may suggest carcinoma. Perforation of the rectal wall not infrequently occurs and a fistulous tract connecting the rectum with the vagina in women and the bladder in men is the result if the perforation is on the anterior wall of the rectum. If the perforation is into the pelvic cavity a pelvic cellulitis is the result which may be acute but more frequently is chronic. . When examined with the proctoscope an ulcerated gumma appears as a crateriform ulcer with hard edges, the floor of the ulcer being covered as a rule with a yellowish necrotic membrane. When touched with a cotton tipped applicator there is always more or less bleeding. It may or may not be painful.

In diffuse gummatous infiltration the tube is more or less thickened and rigid and its lumen is considerably reduced. The mucous membrane appears red and edematous and often shows punctate hemorrhages upon its surface. There is nearly always more or less perirectal infiltration which in rare instances may extend to the pelvic fascia in which event should the patient be a woman the uterus and its appendages and sometimes the bladder may be imbedded as it were in the gummatous deposit and thus strongly suggest malignant disease. Herxheimer has reported five such cases. Gummatous infiltration may involve the entire rectum from O'Bierne's sphincter to the sphincter ani, in some instances the involvement of the internal and external sphincters in the process causes them to lose their tone and involuntary passage of feces may occur. The symptoms in gumma and in gummatous infiltration resemble those of proctitis which in fact it is. There is a feeling of weight in the rectum which causes a desire to defecate at frequent intervals. Defecation is attended with tenesmus and the passage of small amounts of fecal matter or of mucus, or mucus and blood. Hemorrhage from the rectum sometimes occurs if a gumma ulcerates through a vessel. Pain may or may not be present—usually it is, and is felt in the pelvic region and down the thighs. Unless checked by treatment the condition may cause a cachexia to develop which may be mistaken for that of carcinomatosis. In tropical countries and in broken down alcoholics or those suffering with diabetes or chronic nephritis the gummatous process may extend outward and involve the cutaneous surface about the anus and the perineum, and in women, the vulva.

If constitutionally treated gumma and gummatous infiltration yield rapidly and satisfactorily and if treated in time leave naught but slight scars of the rectal mucosa. However if allowed to go on

to fibrous transformation stricture of the rectum almost invariably results. The rectum is transformed into a narrow and rigid tube through which the little finger can only be introduced with difficulty or not at all. The anus in severe cases is relaxed and funnel shaped, the sphincters having lost their power to contract. The stools passed are much smaller than normal—often flat and ribbon-like. Constipation alternates with mucous diarrhea in some cases but not in all—the ribbon-like stools may be the only symptom.

Tertiary syphilis of the rectum is most frequently confused with carcinoma or in some instances with chronic dysentery or colitis. In some instances tertiary syphilis of the rectum may be confused with tuberculosis. Syphilitic rectal disease is however, not as difficult to diagnose as gastric or esophageal. It is much more frequent than either of these latter conditions and the lesions manifest are usually characteristic as to their origin.

Secondary Syphilis of Rectum.—Secondary syphilis of the rectum may occur, although somewhat rarely. Mucous patches within the internal sphincter ani have been observed. They give rise to no symptoms or at most to a mild proctitis which soon disappears. Mucous patches and condylomata lata are not infrequently observed about the anus. Their characteristic appearance leaves no doubt about the diagnosis. Chancre of the anus is sometimes observed. It is usually due to sodomy.

CHAPTER XLI.

SYPHILIS OF THE LUNGS.

Although no tissue of the body is immune to the invasion of the Treponema pallidum, the lungs and the pleuræ are less frequently involved than any other viscera with the exception of the prostate gland. Statistics obtained from autopsies show this to be a fact. In 1898 there were in the museums of the great hospitals of London but 12 specimens of pulmonary syphilis. In 2800 autopsies done at the Johns Hopkins Hospital and reviewed by Osler, there were but 12 cases of pulmonary syphilis and of these 8 were of the congenital type. In 3000 autopsies done at the Massachusetts General Hospital, Lord found only 1 case. In a study of 4880 autopsy protocols, Symmers found syphilitic involvement of the lungs in 12 cases and syphilitic scars of the pleuræ in 2 more. On the face of these returns it is evident that syphilis of the lungs is an extremely rare manifestation of the disease.

While admitting the rarity of lues pulmonum, I am convinced that it is more frequent than is generally supposed. An accurate study of those cases in which the pulmonary lesion was basal instead of apical, with the sputum negative for tubercle bacilli, would, in my opinion, reveal syphilis of the lungs much more frequently than autopsy findings have hitherto shown.

Congenital Syphilis of Lungs.—Congenital syphilis of the lungs has long been known. Even so long ago as the eighteenth century there was a considerable literature on the subject, but it was not until 1853 that an anatomical description of the condition was given by Dupaul, in his classic monograph entitled "A Manifestation of Congenital Syphilis consisting in an Alteration of the Lungs not yet Described." Later, Wagner in his work on "Syphiloma" gave a much fuller description of the congenital form of the disease as well as describing the lesions to be found in the acquired disease.

Shortly after this the great pathologist, Virchow, expressed himself concerning the condition. This he did most guardedly, although he recognized certain lesions of the lungs as probably syphilitic, particularly when present with other manifestations of the disease. The most noteworthy of these is a fibrous, interstitial pneumonic process surrounding the bronchi, from which there arise fibrotic bands which pass along the smaller bronchi and vessels toward the

periphery. These by their subsequent contraction as the chronicity of the condition continues, produce marked deformity of the affected lung. This fibrosis is often associated with a pleurisy by extension of the fibrous process. Gummata may also form, which later break down and lead to the formation of cavities. There may also be caseous formations which are often difficult to distinguish from the gummata.

This description of Virchow formed the basis of many subsequent descriptions of syphilitic disease of the lungs. For a time syphilitic phthisis was uppermost in the minds of many clinicians, much more so, I might add, than it is now. This was perhaps largely due to the general acceptance of the views of Virchow as to the duality of most of the lesions of phthisis.

It is passing strange that syphilis of the lungs should be the rare condition that many seem to consider it. That the lungs are so frequently attacked by the tubercle bacilli we can readily understand because of the ease and facility with which the organisms can enter them. While it is not to be supposed that the Treponema pallidum would be apt to enter the lungs from the bronchi except in syphilitic ulcerative bronchitis—a condition which undoubtedly exists—yet it is reasonable to suppose that the lungs are equally exposed to the penetration of the organisms as other organs—the liver for example.

In 1891, Councilman reported two cases of patients with syphilis of the lungs who during the two preceding years had died in the Johns Hopkins Hospital. Both of these were extremely typical of lues pulmonum. One of them owing to the extent and the acuteness of the lesions offered a unique opportunity for the study of the condition. In both autopsies were made and sections of the diseased lungs were stained and examined for tubercle bacilli, as this occurred before the days of the Wassermann or the Treponema pallidum. Tubercle bacilli were not present, but an interesting feature of the investigation was the hyaline degeneration of the capillaries. While it would be hardly possible to assert that this hyaline degeneration is absolutely distinctive of pulmonary syphilis, yet its presence is, at least, highly suggestive of it. Hall reported a case in which there was demonstrated a syphilitic ulceration in the left bronchus at the point of bifurcation which gave rise to severe attacks of hemoptysis extending over a period of a dozen years or more. In 1914, Blinder reported a case which was mistaken for pulmonary tuberculosis for over a year. Repeated negative results in the sputum for tubercle bacilli and the situation of the lesion at the base of the lung, caused an inquiry to be made as to the presence of syphilis. The history of a primary lesion was obtained and also a positive Wassermann; antisyphilitic treatment was then instituted, and the quick response and ultimate recovery

of the patient proved conclusively that syphilis was the causative factor although the cardinal symptoms of pulmonary tuberculosis with the exceptions noted were present to a marked degree. In 1915, Levin of New Orleans reported 2 cases. In 1 there was hemoptysis, fever of the hectic type and profuse mucopurulent expectoration. A diagnosis of abscess of the lung which was later changed to that of tuberculosis was made. The patient was sent to a sanitarium where the true nature of the disease was discovered and cured by antisyphilitic treatment. The chief symptom of the second patient was hemoptysis. The lesion in this instance being located at the apex instead of at the base where most syphilitic lesions of the lung are found. A gumma of the clavicle and a positive Wassermann proved syphilis to be present, and under treatment the pulmonary lesion also disappeared.

Seven cases of pulmonary syphilis were reported by Lisser in 1918. His opinion is, and with it I concur, that syphilis of the lung is uncommon but no so extremely rare as most text books would infer.

From this brief résumé of cases reported by very competent observers it is possible to establish the fact that syphilis of the organs of respiration occurs rather infrequently, also that it is quite possible that this frequency would be notably increased if the diagnosis was not so often confused with that of tuberculosis. The presence of a positive Wassermann here is not of such material aid in diagnosis as it ofttimes is elsewhere. While it of course indicates that the patient has syphilis it does not necessarily imply that the pulmonary condition is luetic. The infrequency of this manifestation of syphilis and the well-known fact that antisyphilitic treatment, especially mercury and potassium iodide, has a very deleterious effect upon phthisical patients will give pause to most physicians in diagnosing syphilis of the lungs unless based upon very solid reasons.

It is well, therefore, to inquire deeply into these cases and to have the clinical facts thoroughly established before reaching a conclusion. Syphilis of the lung does not exhibit a typical clinical picture and this also includes roentgenography which is such a powerful aid in the diagnosis of pulmonary tuberculosis. These are of value more in a negative sense in that they are of decided help in excluding pulmonary tuberculosis—the condition with which lung syphilis is most apt to be confused. Also, it must always be remembered that the two conditions may exist simultaneously.

Signs and Symptoms.—As a rule the pulmonary syphilitic lacks that indefinable something which is characteristic of the tuberculous patient. For instance, in pulmonary syphilis, the clubbing of the fingers, so often seen in tuberculosis, is usually absent. The chest is better shaped, that is, the transverse diameter may not be

so marked as it is in the tuberculous, which gives the characteristic flat appearance to the thorax. The breathing may not be as shallow as it is in phthisis. An important sign is the pulse. The characteristic rapid, thready pulse of low tension, so frequently noted in pulmonary tuberculosis, is nearly always absent in pulmonary syphilis. If there is fever, as there frequently is in syphilitic lung disease, the pulse will be accelerated but not to the extent that it is in pulmonary tuberculosis. In pulmonary tuberculosis there is more or less emaciation. In pulmonary syphilis the patient may appear remarkably well nourished, so much so that the signs in the lungs and the physical appearance of the patient are in most marked contrast. Dyspnea, always present in phthisis, may be absent in pulmonary syphilis, although it is sometimes present and may confuse the examiner. Night sweats are also present at times as in phthisis. Profuse expectoration which may be fetid is commonly present. Tubercle bacilli are absent but the Treponema pallidum may be present. Hemoptysis is very frequently present and this symptom must be considered in those unusual cases where pulmonary syphilis is suspected. Fever is usually present in pulmonary syphilis but the temperature is never high and the difference between the morning fall and the evening rise is not so marked as it usually is in pulmonary tuberculosis.

Consolidation.—Consolidation in pulmonary syphilis is rarely noted at the apex as in pulmonary tuberculosis. Also in pulmonary syphilis the area of consolidation may be limited to one lung and the other be entirely free of any signs whatsoever. This is rare in tuberculosis of the lungs, where, even if one lung is much involved, there is almost invariably a small area at least of consolidation in the less affected lung. This, coupled with the absence of the tubercle bacilli in the sputum and a positive Wassermann and possibly other evidences of luetic disease, should give rise to the suspicion, at least, of pulmonary syphilis.

Types of Syphilis of the Lung.—Syphilis of the lungs may be divided into two types: an ulcerative tracheo-bronchitis, and gummatous formations in the deeper portions of the lungs. Each of these types of lesions has its own particular symptoms. In ulcerative tracheo-bronchitis there is cough which is usually paroxysmal. Not infrequently it has the peculiar brassy sound which is associated with the cough of aneurysm. Attacks of dyspnea frequently supervene. These alternate with breathing that is perfectly normal. Frequently there is hoarseness or even aphonia. Stridor may be present and drawing in of the supraclavicular and infraclavicular spaces upon inspiration. This form of lung syphilis is more apt to be confused with aneurysm than with pulmonary tuberculous disease. A point of distinction, however, is that in

this form of pulmonary syphilis there is no inequality of the pulse, which is almost sure to be present in aneurysm.

In syphilis of the deeper portion of the lung the resemblance to pulmonary tuberculosis is closer. If there is a widespread infiltration which precedes gumma formation there will be the characteristic dulness observable also in consolidated areas in tuberculosis. In consequence of this diminution in the volume of the lung there will be corresponding dyspnea. If the area of infiltration is slight, the dyspnea will be slight; if it is large, the dyspnea will also be large. In these cases cough is usually present and, in the early stages, may be of an irritative types and not attended with much expectoration. Later when the infiltrated area breaks down the expectoration may be profuse and if a vessel is encroached upon by the process as in tuberculosis, hemoptysis, which may be profuse as in tuberculosis, may also be present. As would naturally happen in such a condition other organisms enter into the diseased areas and a mixed infection is the result, as in tuberculosis, consequently fever is also present and other evidences of a low grade of chronic sepsis such as sweats, chills, flushes, headache and disordered digestion, all of which symptoms from the same cause are also met with in pulmonary tuberculosis. Loss of weight and strength may also occur but not so frequently as in pulmonary tuberculosis. As I have already stated, the patient may appear remarkably robust and well nourished, a strong contrast to what is observed in tuberculous pulmonary disease.

The physical signs as well as the symptoms of pulmonary syphilis are never characteristic or distinctive, the physical signs, of course, being dependent upon the nature of the lesions. Roentgenograms are often disappointing. They portray nothing characteristic. As I have already said, they are of value only in a negative sense, in that they help to exclude pulmonary tuberculosis. The roentgenogram of a luetic lung is quite unlike that of tuberculosis, in that it is denser and shows a more compact picture, as it were, and if gummata are present they are not infrequently mistaken for tumors. An extensive hilus shadow with outrunners is the picture which is most apt to indicate the luetic disease. The shadows in pulmonary syphilis are less distinct than is the case in pulmonary tuberculosis. It is also well to remember that, in syphilis of the lungs, cavity formation is very rare.

Diagnosis.—The diagnosis of pulmonary syphilis is made by exclusion. Tuberculosis must be ruled out, also actinomycosis, glanders and streptothricosis; it must also be remembered that infiltration of the lungs occurs occasionally in leukemia and Hodgkin's disease. These last conditions are so rarely encountered that it can hardly be said that they enter into the problem at all. In

order to exclude tuberculosis it is necessary to resort to every possible test and to weigh carefully the evidence of each test in its bearing on the condition. A Wassermann test must be made, although in this connection it must constantly be borne in mind that syphilis and tuberculosis may be present simultaneously. A von Pirquet test should be made and the sputum should be examined both for tubercle bacilli and the Treponema pallidum. If the last is found the evidence is conclusive.

I agree with Fowler that more is to be learned from the examination of the sputum than from the physical examination. Pulmonary syphilis should not be diagnosed simply because a lesion has antunusual situation. When the physical signs denote a stenosis of he trachea or of one of the large bronchi, if aneurysm can be ruled out, the probability of syphilis is much increased. Syphilis of other viscera should be searched for. It is also well to remember that syphilis of the lungs develops much more slowly than tuberculosis except that form of chronic fibrosis of the lung, known as fibroid phthisis and which, as I have stated elsewhere, is in my opinion sometimes due to the Treponema pallidum rather than the tubercle bacillus.

In a general way syphilis of the lung is apt to be circumscribed rather than disseminated. It is less apt to begin at the apex, as does tuberculosis, but this is by no means invariable; and while this sign carries weight, too much significance should not be given to it. Pulmonary syphilis is most apt to be found in the vicinity of the hilum as is often noted in radiograms.

Gummata of Lung.—Gummata of the lung are similar to gummata occurring elsewhere. They range in size from a millet seed to that of a hen's egg or even larger. They may occur anywhere in the lung but as in the infiltrative form of the disease are most apt to occur near to the hilum. Upon postmortem examination they are in the early stages of their development of a grayish-white or grayish-yellow color, somewhat translucent and surrounded by a zone of congestion. Later they become more opaque and may even caseate and, should they empty into a bronchus, their contents will be coughed up and a cavity is thus formed. This last is rare, however, as they usually become fibrous and the consequent shrinking may cause considerable deformity of the lung with adherence of the pleural surface.

Syphilis may manifest itself as bronchopneumonia. It is most frequently a termination of the life of syphilitic children and infants in whom the disease has been severe from the onset. Occasionally it occurs in adults and then cannot be distinguished from that arising from any of the other causes which give rise to the disease. Such cases have been described by Delepine and Sisley and by Pavlinoff.

Chronic Interstitial Pneumonia.—Fibroid induration or chronic interstitial pneumonia is another type of pulmonary syphilis. This type is more frequently confused with the tuberculous type than any other form. The inflammation takes the form of an extensive cellular infiltration, together with an overgrowth of the connective tissue of the interlobular and intralobular septa, and a proliferation and desquamation of the alveolar epithelium. The alveolar walls and the capillary walls are greatly thickened. The result of this fibrosis is that long strands of fibrotic tissue radiate from the hilum and more or less surround the bronchi and the bloodvessels. Not infrequently they bind down the pleuræ and divide the lobes by constricting bands. The signs and symptoms of this form of pulmonary syphilis do not differ from fibroid phthisis.

Syphilis of the lungs, except as it occurs in congenital syphilis, is essentially a tertiary manifestation of the disease, although syphilis of the lungs has been recorded as early as one year after infection. This does not mean, however, except in point of time, that the lesion was not of a tertiary character, as tertiary type lesions may occur almost at any time after the initial lesion. Several observers have noted the condition only a few months after the infection (Frank in 1880 and Schirren in 1875).

It must always be remembered that syphilis of the lung may exist without the patient or the physician being aware of it. It may exist for years without causing any symptoms whatsoever. As has been stated by Bazin, "The victims of pulmonary syphilis eat their food and walk about like people in good health; their expectoration is slight and grayish, their cough and dyspnea not marked." This state of affairs may continue for years, interrupted now and then by attacks of bronchitis. Or, it may terminate in bronchopneumonia. This latent type of the disease may simulate early tuberculosis very closely, and indeed, is usually mistaken for it. There may again exist types of pulmonary syphilis in which the only manifestation of the disease is in the lungs. Landis has recorded five such cases.

In 1917 Warthin demonstrated syphilitic disease of the pulmonary artery with beginning aneurysm. To my knowledge this is the first time this condition has been demonstrated. Undoubtedly it has existed before, and will in the future be observed from time to time.

Congenital Syphilis of Lungs.—Congenital syphilis of the pulmonary type is the manifestation of pulmonary syphilis of which most is known. For the most part this type of pulmonary syphilis is of pathological interest only, as few of these patients survive more than a month or so. The pulmonary lesions are almost invariably accompanied with other evidences of the disease. There is no definite symptomatology. There may be deficient resonance

in some part of the chest. Cyanosis and dyspnea are present and increase until death occurs. The chances of saving the life of such an infant even under the most skilful treatment are very small.

White Pneumonia.—The condition known as white pneumonia, first described by Virchow, is found in the lungs of still-born infants or of those who have lived but a few hours after birth. The infant usually shows other evidences of syphilis. These lungs are either entirely airless or deficient in floating power. The lungs are increased in size and show the marks of the ribs on their surface. On section the lungs are of a mottled gray appearance not unlike that of the pancreas. Large numbers of the Treponemata pallidum can be found. Interstitial pneumonia terminates the lives of many of these infants in a few days. It is nothing more than a more advanced form of the white pneumonia. The lungs are large and hard and grayish in color. Both lungs may be affected or a single lobe or portion of a lobe. The interlobular connective tissue is much increased, which gives a toughness to the organ which the normal lung does not have. Gummata have been observed on autopsy of syphilitic infants dying shortly after birth. These do not differ from those observed in the acquired form of the disease.

Prognosis.—The prognosis of pulmonary syphilis is good. The way these cases respond to treatment is sometimes marvelous. The fibrotic type, however, offers little chance of recovery, as there is no possibility of absorbing the fibrotic tissue. The damage has been done and cannot be undone. Along with antisyphilitic treatment these patients should also receive the building up treatment used in tuberculosis, that is: cod-liver oil, fresh air, rest and such hygienic measures as will increase the bodily strength and resistance.

CHAPTER XLII.

SYPHILIS AND DISEASES OF THE ENDOCRINE GLANDS.

Our knowledge of diseases of the endocrine glands is comparatively recent. This is mainly due to the fact that our knowledge of the functions of these glands has only been developed within the past few decades, and indeed, many questions pertaining thereto are still under discussion. However, we have progressed so far as to realize the importance of these glands in their hypofunction, hyperfunction and dysfunction in causing various dyscrasias concerning which we formerly disguised our ignorance by the more or less euphonious term of idiopathic. It is the relation of syphilis to diseases of the glands of internal secretion that I propose to discuss in this chapter.

Thyroid Gland.—The gland which seems to be most open to the attack of syphilis is the thyroid. It has been stated by Reimers that approximately 50 per cent of syphilitics in the secondary stage of the disease show more or less swelling of this gland. I am not prepared to give unqualified support to this statement but I know that it is extremely frequent, especially in females who have recently become infected. This enlargement usually disappears under treatment and the incident in the pathologic sense is closed. Rarely the tumefaction persists and the symptoms of Basedow's syndrome develop. The fact of the enlargement of the thyroid in women is peculiar in that it is held by some that the thyroid cannot harbor the Treponema pallidum because of the iodine secretion which in women is much greater than in men. Indeed, there are those who go so far as to assert that this hyperactivity of the gland in females as compared to males is why nervous syphilis is less frequently encountered in women than in men. Strange as it may seem when this opinion is considered, most of the cases recorded have been in women. The first case reported in which the nature of the disease was confirmed by histologic findings was in a woman. This was by Barth and Gombault in 1884.

While the thyroid is the most frequently attacked of the endocrine glands by the syphilitic infection, it is by no means common, although the classic Basedow's syndrome is in my opinion more frequently of syphilitic origin than is usually supposed. Syphilis

of the thyroid may be manifest either as a hyperplasia of the glandular elements and their supportive stroma or as a gumma. It may occur in the secondary or the tertiary stages, or congenitally, as reported by Pellegrini and by Demme. Gummata of the thyroid in infants with congenital syphilis were observed by Demme at necropsy. He describes them as being of a size sufficiently large to be noted by the naked eye—of a grayish-yellow color and sharply demarcated like a tuberculous or malignant nodule. Gummata were also found in the liver and spleen. During life the eruption had been pustular, indicating a severe form of the disease.

The thyroid gland is supposed to control iodine metabolism and the intracellular protein metabolism. Its action may be said to be general, as its oversecretion emphasizes the normal activity of all the tissues. There is undoubtedly a close alliance between the thyroid and the vegetative nervous system. The thyroid autacoid also augments the action of the other autacoids, including that of the adrenals.

Hyperthyroidism.—There are two types of thyroid hypersecretion: the sympathicotonic and the vagotonic. In the former there is exophthalmos, tachycardia and mental irritability. In these cases it is also often noted that the skin has a peculiar dryness and alopecia is present; alimentary glycosuria is frequent. In the latter, exophthalmos is not seen and the cardiac rhythm is only slightly accelerated if at all, but symptoms of digestive disturbance are much more prominent. The two types of disturbance may be distinguished by the following: in the sympathicotonic, Graefe's sign is negative—disassociation between the movements of the upper lid and the eyeball; Loewi's sign is positive—epinephrin mydriasis; Moebius' sign is positive—insufficiency of convergence. In the vagotonic type Graefe's sign is positive and the Loewi and Moebius signs are negative.

The literature on hyperthyroidism caused by syphilis is not extensive but there is no question of its occurrence, perhaps more frequently than is supposed. For, we know that all infections cause an oversecretion of the gland and it is very plausible that such a chronic infection as syphilis should have this effect to a marked degree. In support of this Levy-Franckel reports eighteen cases of Graves' disease that developed late in the course of secondary syphilis. Cases have also been reported by Poncet and Leriche in France and by Hazen and others in this country.

Gummata of the thyroid have been reported by Fraenkel, Kuttner, Kohler, Pospelow-Moskau, Clarke and Thompson.

The clinical picture of syphilis of the thyroid may present nothing more than a tumefaction or enlargement of the gland. If however, one or more gummatous masses are present the enlargement may be

irregular. In some cases, but not in all, the classical symptoms of Graves' or Basedow's disease are present. The gland may be so increased in size as to cause pressure symptoms of hoarseness and cough.

Hypothyroidism.—In contradistinction to an overactivity of the gland a condition of underactivity or hypothyroidism may occur. This establishes the clinical syndrome known as myxedema, cretinism or mongolism.

Cretinism.—Cretinism is essentially a disease of childhood and early adolescence; when occurring in adults it is known as myxedema or Gull's disease. It is due to retrogressive changes in the gland such as are caused by fibrosis. The symptoms may be most severe, or so slight that they are overlooked. The last condition is known as Kocher's thyropenia, or the submyxedema of Cobb.

When fully developed, the appearance of these unfortunate patients is characteristic. The skin is dry and leathery. The face is broad like a Chinaman's. The expression is stupid which is but a reflection of the mental hebetude. The pulse is slow and the blood-pressure is below normal; the temperature is also subnormal. In females there is amenorrhea, and impotence in males.

In the infantile form there are usually no evidences at birth, but the diathesis manifests itself within a few months by the infant sleeping more than is usual and by becoming excessively fat. Soon the tongue appears to be too large for the mouth and it protrudes. There is an excessive flow of saliva—drooling. The mental development is greatly retarded. The fontanelles close late. As the child grows older its develops unevenly. The head is too large. The body is short and squat—it lacks the slenderness of youth but is obese and paunchy. Unbilical hernia is frequent. These children are extremely typical. They are a burden to themselves and others.

That congenital syphilis can produce this melancholy state there is no reason to doubt. In many instances, especially when the condition becomes manifest in the early months of infancy, I am convinced that the pathologic process originated *in utero*.

All cases of thyroid disturbance should arouse a suspicion of syphilis as the determining factor. No operation should, in my opinion, be performed for a removal of a part of the gland until a Wassermann test has been made. The therapeutic test should also be made; especially the administration of large doses of potassium iodide. Gummata of the thyroid frequently disappear with remarkable rapidity—even more so than with arsphenamine—under the influence of this drug.

Parathyroid Glands.—After careful search I have been unable to find any mention of syphilis affecting the parathyroid glands. It is possible however, in my opinion, that some cases of tetany are due

to syphilitic involvement of these glands. In not a few instances, I believe, the convulsions to which congenitally syphilitic children are predisposed are due to an unrecognized involvement of the parathyroids.

Pancreas.—Next in frequency to the thyroid, the pancreas is involved in syphilis of the endocrine glands. This condition is not frequent, or perhaps, I had better say, it is not frequently diagnosed. In support of this is the evidence offered by Warthin of Ann Arbor. In a large series of cases which came to autopsy he found the pancreas involved in every instance. A further detailed study of six cases of diabetes of syphilitic origin upon which necropsies were made showed various changes in the gland, including atrophy due to the formation of fibrous tissue. This fibrosis was interlobular and intralobular and caused the glandular elements to undergo atrophy or fatty degeneration. The islands of Langerhans were diminished in size and the acini were larger than normal. Warthin also observed similar changes in the pancreatic gland of syphilitics at necropsy in whom diabetes was not present. He therefore suggests that associated changes in the liver, adrenals and the pituitary body may be necessary to complete the endocrinic syndrome of diabetes. I am of the opinion however, that disease of the pancreas alone can also produce glycosuria.

Syphilitic Pancreatitis.—The symptoms of syphilitic pancreatitis differ but little from those due to some other cause. There is pain in the epigastrium with tenderness on pressure. The pain may be stabbing in character and at times suggest the pains of biliary colic. The stools are bulky and of a buttery consistency due to undigested fats and proteids. In some cases there is a discoloration of the skin —the so-called bronzed diabetes. If there is a gumma of large size situated in the gland there will be somatic signs which will help in the clinical diagnosis. If the neoplasm exerts pressure on the bile duct there will be jaundice; if on the portal veins there will be ascites and hemorrhoids; if on the inferior vena cava there will be edema of the lower extremities; if on the left ureter there will be hydronephrosis. Gastro-duodenal or colonic symptoms are apt to be present. Persistent jaundice accompanied with a palpable gall-bladder and a positive Wassermann reaction is always suggestive of syphilitic involvement of the pancreas.

Spleen.—The spleen is frequently enlarged in the early secondary stage of syphilis; although, in my opinion, this enlargement is not encountered with the regularity asserted by some. Enlargement of the spleen when it occurs will usually be found in those patients who were anemic when the disease was contracted. As the patient's health improves and the anemia disappears the splenic swelling also passes away. In the tertiary stage gumma may occur or there may

be a hyperplasia of the connective tissue stroma which later contracts so that the organ is ultimately reduced in size. Amyloid changes may supervene, which may be diffuse or limited to the Malphigian bodies. This form of syphilitic splenic disease is frequently associated with amyloid changes in the liver and kidneys and with disease of the bones and with gummatous infiltration of the rectum. In congenital syphilis splenomegaly is often observed and the organ may reach an enormous size.

Adrenal Glands.—Syphilis of the adrenal glands presents the clinical syndrome known as Addison's disease or melasma suprarenale; this latter condition not infrequently has syphilis for its exciting cause. The glands may undergo amyloid degeneration or an interstitial fibrosis or gumma may form. When gummata occur they are most apt to be of the miliary type. Melasma suprarenale caused by syphilis has been reported by Fordyce and by Jacquet and Sezary. The condition known as Addisonism, which is usually congenital, I have already mentioned.

Changes in Secondary Sexual Characteristics.—A strange dystrophy, said to be the result of tumors or hyperplasia of the cortex of these glands is change in the secondary sexual characteristics. These changes may be observed in infantile life or they may take place slowly before adolescence, or, rarely, they may occur in adult life. Females are more frequently affected than males. The condition known as pseudohermaphroditism is an example of these changes. Congenital syphilis attacking the adrenal cortices is the most probable explanation and this applies to the late forms of perversion as well. When they occur after puberty they probably represent a delayed manifestation of the congenital disease. It is possible however that they may be due to the acquired disease in its tertiary form as a gumma or fibrosis.

Sexual Glands.—In the tertiary stage of syphilis the testicles are frequently attacked. The same is probably true of the ovaries. Our knowledge of syphilitic disease of the last named however, is slight. The gross pathology of syphilis of the testicles I have discussed elsewhere. In so far as the perversion of these so-called gonad glands are concerned, as to hyperfunction or hypofunction, any bearing that syphilis may have is practically unknown. It has been said that syphilis increases sexual desire in women, but if it does I have not observed it and I have had abundant opportunity for so doing. Taylor and others have asserted that syphilis is a cause of sterility in both males and females. My personal experience does not include this. I do not believe that acquired syphilis *per se* in any way alters the functions of these glands except mechanically as a result of sclerosis of the ovaries, or a destructive gumma or fibrosis of one or both testicles. Syphilis probably acts

upon the gonad glands, but it acts remotely in that it may give rise to a congenital syphilitic dystrophy or one in the second or third generation. Examples of this would be *pubertas præcox* in males and *menstruatio præcox* in females, or the opposite extreme of infantalism or underdevelopment. All of these are indicative of what is broadly termed "degeneration," of which I believe syphilis, even more than alcoholism, is the cause.[1]

Pituitary Gland.—But little is known of acquired syphilis of the pituitary gland, and whether it is influenced by congenital syphilis we know nothing at all. Gummata of the gland have been reported and in these instances the symptoms have resembled very closely those which would be produced by an intracranial tumor due to some other cause. Vomiting, dizziness and mental apathy are prominent symptoms. Epileptoid attacks may occur. Disturbance of vision is frequently present; this is usually bilateral and includes choked disk, optic atrophy and some form of scotoma. Spastic paralysis with a positive Babinski may be present. Polyuria is usually a prominent symptom. The syndrome known as acromegaly or gigantism is pathognomonic of pituitary involvement whether due to syphilis or not. It is more frequently observed in females than in males and usually appears before the fourth decade of life. The roentgen ray shows the gland to be enlarged and the sella turcica eroded; this, with diabetes insipidus, as pointed out by Barker, and a positive Wassermann reaction in the blood and spinal fluid, with perhaps some of the other symptoms mentioned, will, in most instances confirm the diagnosis.

Pineal Gland.—The pineal gland may be attacked by syphilis in the tertiary stage. Very few cases have been reported and these are vague. The secretion of this gland is supposed to exert an influence upon the mental and bodily development, although our knowledge of its physiology is extremely limited. When the gland is diseased the symptoms are those referable to intracranial pressure and consequently include headache and vertigo, focal vomiting, choked disk and mental dullness. Polyuria and polydipsia are usually present.

From this short sketch it can be readily appreciated how closely interrelated endocrinology is with neurology and neurology with syphilology. As the work on vegetative neurology widens in scope and our knowledge thereof increases it will become more and more evident that the activities of the ductless glands are closely associated with the action of the vagus and sympathetic nervous system. The pathologic hiatus which now exists between them will be found to be filled, I believe, by the subtle toxemia of syphilitic infection.

[1] Syphilis and Degeneration, by Burton Peter Thom M. D., The Journal of Nervous and Mental Diseases, January, 1921, **53**, No. 1.

This opinion, I may say, is shared by many other clinicians. Since our knowledge of this phase of syphilis is so lacking, the syphilitic basis of the endocrinopathies offers a most fertile field for research and one which in the years to come will undoubtedly be developed to a high degree, and our present inadequate knowledge of these high governors of the body's chemistry will be increased manifold. Thus will be penetrated the last of the mysteries of physiology and pathology.

CHAPTER XLIII.

SYPHILIS OF THE EYE.

The complex and delicate mechanism of the eye is frequently attacked by inflammatory or degenerative processes the result of syphilis either congenital or acquired. The opinion of Bulson, that from 50 to 60 per cent of all eye diseases are due to syphilis I believe to be true.

Chancre of the Eyelid.—Chancre of the eyelid sometimes occurs; but this is rather a rare site for the extragenital lesion. It may be on either the upper or lower lid, usually near the inner canthus. When we consider the multiplicity of possible means whereby syphilitic infection can occur, the rarity of the primary sclerosis of the ocular apparatus, is, to say the least, surprising. Hirschberg believes that primary infection through the eye usually comes from kissing and the habit, especially among the lower classes, of moistening the agglutinated lids of infants in order that they may open them; also the practice of removing with the tongue foreign particles which have found lodgement in the eye.

Chancre of the eyelid begins as a small circumscribed elevation which may at first be with difficulty distinguished from hordeolum or chalazion. A cup-shaped ulcer forms because of necrotic changes in the center and the base becomes indurated. This induration in time assumes the cartilaginous hardness characteristic of the initial sore. In not a few instances however, this hardness does not appear, and for that reason the diagnosis is rendered more difficult. These lesions are rarely painful but the edema of the eyelid and the irritation of the cornea may cause much discomfort. The lymph glands at the angle of the jaw and in front of the ear are invariably enlarged and hard, and their involvement should be considered in making a diagnosis. A chancre may occur on the conjunctiva, either on the palpebral or ocular surfaces; primary lesions so situated however, are extremely rare.

Syphilitic Conjunctivitis.—In the eruptive stage of the disease papules sometimes appear on the conjunctiva and the palpebral edges. The irritation caused thereby may give rise to a syphilitic conjunctivitis. Should the condition persist granulations may form not unlike those seen in trachoma.

Syphilitic Iritis.—The most frequent ocular lesion of secondary syphilis is iritis. Rarely it appears in the tertiary stage but I

believe that a considerable number of so-called iritides in the tertiary stage are really gumma of the iris. Iritis can also occur as a congenital manifestation and when it does it usually runs an acute course. Photophobia and pain, which, as in many other syphilitic processes is always worse at night, are the two symptoms concerning which the patient complains most. The vision is more or less impaired owing to the exudate concomitant with the affection. This exudate, unless prevented by instillations of atropine, rapidly organizes and forms adhesions which distort the iris and cause it to adhere to the anterior capsule of the lens. The color of the iris changes, becoming greenish in blue or gray irides and muddy in darker varieties. The pupillary margin becomes thickened and shows yellowish nodules the size of a pin head or even larger. With syphilitic iritis there is often involvement of the posterior portion of the eyeball—the choroid, retina and optic nerve. As a rule one eye is attacked first and the other becomes affected shortly after.

Syphilitic Choroiditis.—Choroiditis, next perhaps to iritis and keratitis, is the most frequent ocular disease caused by syphilis. It is nearly always a secondary manifestation but it may occur in the tertiary stage. There are no objective symptoms discernible without the aid of the ophthalmoscope and the process is not attended with pain unless the iris or ciliary body is involved. The patient usually consults the physician because of disturbances of vision. These consist in diminished acuity, distortion of objects, which may appear too small or too large—as a result of the displacement of the retinal elements over the inflamed focus—flashes of light and restriction of the field of vision—scotoma. The ophthalmoscope reveals a characteristic picture of exudative patches of a yellowish-gray color, opacities of the vitreous and hyperemia of the optic disk. Other parts of the ocular apparatus are also frequently involved—the iris, retina, vitreous, optic nerve and sclera.

Syphilitic Retinitis.—The retina is frequently affected in secondary syphilis. It occurs less frequently as a lesion of congenital syphilis. The retinitis of acquired syphilis differs somewhat from that of congenital syphilis which usually is seen after the subsidence of a keratitis. Secondary syphilitic retinitis is frequently associated with choroiditis and iritis. The signs of the disease are obtainable only by means of the ophthalmoscope and consist of cloudiness of the fundus due to edema of the retina and disk. Minute opacities are observed on the posterior portion of the vitreous and it is these opacites which cause the disk to appear red and hazy. In the macular region are to be seen circumscribed white patches which may also be pigmented on their borders. The patient usually complains of dimness of vision, although photophobia may also be

present. Other symptoms are contracted vision, flashes of light and especially night blindness. The last mentioned symptom, I may say, if the patient also complains of dimmed or distorted vision, should always cause the physician to suspect retinitis.

In the congenital form, the fundus when examined through the ophthalmoscope is of a brown or grayish color with patches of pigment or white spots thereon, most of which are situated at the periphery. Unless properly treated retinitis may lead to atrophy of the retina and of the optic nerve—blindness.

Syphilis of the Sclera.—The sclera is sometimes attacked by syphilis in the secondary stage; rarely, it is the site of a gumma in the tertiary stage. The inflammation thus developed may be of the superficial type known as episcleritis in which the superficial tissues alone are involved, or the entire sclera and the subjacent and contiguous parts may be affected. The process is attended with symptoms of irritation causing lacrimation and the sclera and conjunctiva are congested. A raised patch, of a deep red color is to be seen in the ciliary region, usually on the temporal side. This patch disappears under treatment but is prone to come again in another spot in proximity to the first, and these recurrent nodes may in time completely encircle the cornea. The condition may resemble phlyctenular conjunctivitis very closely.

Tertiary Syphilis of the Eye.—The lesions I have described represent the most common syphilitic processes affecting the eye. They nearly all occur as secondary manifestations. However, they may not appear until many years after the initial lesion and in point of time may then be classed as tertiary. Since the gumma is the characteristic lesion of that stage, many of these lesions when occurring late in the disease may be pathologically classed as such. Some lesions are distinctively tertiary and of these may be mentioned tarsitis gummosa or gummatous infiltration of the eyelids. The tarsi may become so swollen from the gummatous infiltration that it is impossible to evert the lids. Periostitis of the bones composing the cavity of the orbit sometimes occurs in tertiary syphilis. The pain is deep seated, is worse at night, and is augmented by pressure on the eyeball. Gummatous infiltration of the lacrimal sac and nasal duct is sometimes observed. The sac and duct may be obliterated. Paralysis of one or more of the extrinsic muscles of the eye due to a syphilitic meningitis of the base is frequently met with in cerebral syphilis. These paralyses may be said to be almost pathognomonic, as three-fourths of them are due to syphilis. Toxemias such as rheumatism, influenza and diabetes account for the remaining fourth.

I can hardly conclude the discussion of tertiary syphilis of the ocular apparatus without passing mention, at least, of reflex irido-

plegia or the Argyll-Robertson pupil, the almost constant concomitant of tabes and paresis. The pupil in this instance contracts with accommodation and convergence but does not respond to light. This is due to an interruption in the path from the optic nerve to the oculomotor nucleus, the connections of the centers for accomodation and convergence remaining unaffected. These too however, are sometimes affected and in the tabetic or paretic eye accomodation and convergence may also be lost. The changes causing this condition are not, in my opinion, due to a primary optic atrophy but rather to an inaugurating gummatous infiltration and which at first appears, if discovered early enough, as a papillitis.

Eye Lesions in Congenital Syphilis.—Lesions determined by congenital syphilis frequently affect the eye. Of these the most frequent and characteristic is keratitis. So much so is this that the opacities remaining therefrom should always arouse the suspicion of congenital syphilis. When due to congenital syphilis the process usually manifests itself between the fifth and fifteenth years. It may appear as early as the third year. De Schweinitz is of the opinion that it may occur *in utero*. It is rarely encountered as a congenital symptom after the thirtieth year. Should it occur thereafter it is quite possible that it is tertiary as in about 10 per cent of all cases it is due to acquired syphilis. It is more frequent in females than in males.

The inflammation begins either at the margin of the cornea or in the center. If it begins in the center of the cornea there will be observed a grayish infiltration which spreads peripherally. If it begins at the margin of the cornea, one or more grayish spots will be observed which gradually coalesce and implicate the whole cornea. When the inflammation has spread over the entire corneal area, it imparts to it a dense grayish or even yellowish color, so that the iris can be seen only with difficulty, and vision is reduced to little more than the perception of light. At this stage the cornea has a ground-glass appearance and small bloodvessels appear, derived from the anterior ciliary artery. All this gives rise to considerable irritation which causes increased lacrimal flow. Ulceration rarely occurs, but the iris is frequently involved, also the ciliary body and the choroid. After the cornea has become less opaque, evidences of the accessory inflammations will be observed in the form of adhesions of the iris to the lens—posterior synechiæ, changes in the iris and choroid, opacities of the vitreous and even occlusion and exclusion of the pupil. Keratectasia, or protrusion of the cornea may follow. Dense opacity may also follow so that vision is almost or entirely lost. Both eyes are usually involved, the inflammation commencing in the sound eye before the inflammation has subsided in the one first affected.

As a rule children who have had interstitial keratitis show other evidences of congenital syphilis—the saddle nose, the radiating scars at the angles of the mouth, Hutchinson's teeth—puny bodies and waxy, sallow complexion.

The keratitis of acquired syphilis is usually a tertiary manifestation or a late secondary. It is more amenable to treatment than the congenital type and less apt to leave.

The ocular lesions observed in acquired syphilis may also occur in the congenital form and when they do so are apt to be more rebellious to treatment. Mention might be made of a form of tarsitis occurring in infantile life due to congenital syphilis. It may resemble a chronic blepharitis with the formation of crusts and ulcers at the mouths of the follicles of the eyelashes. A permanent thickening of the tarsi may follow. Absence of the eyelashes in children should always cause a suspicion of congenital syphilis. It is also well to remember that eyes which have been affected by congenital syphilis are particularly prone to tuberculous infection in later years.

CHAPTER XLIV.

SYPHILIS OF THE EAR.

The apparatus of hearing is frequently attacked by syphilis. Not only does this occur in the acquired form of the disease but also in congenital syphilis. Because of this frequency and the serious damage arising therefrom in many instances, a correct understanding of these lesions is of very great importance.

External Ear.—Primary lesions occurring on the external ear have been reported but of necessity such lesions are extraordinarily rare. The same is now true of chancre of the Eustachian orifice. Formerly however, before the days of instrumental sterilization, Eustachian chancre was not uncommon. Macular, papular and tubercular lesions in the eruptive stage of the disease are not infrequently observed on the external ear. Sometimes they invade the auditory canal and secondary eruptions have been observed on the membrana tympani. Condylomata of the external meatus are encountered with comparative frequency in secondary syphilis. These warty growths are perhaps the most frequent of the external manifestations of syphilis of the ear. Their development is favored by a pre-existing otorrhea or eczema or the discharge from a syphilitic catarrh of the tympanic mucosa. The meatus may be entirely occluded by the swelling from which is exuded a foul smelling secretion. Pain is present and may be severe especially in moving the jaws as in eating or talking. There is apt to be considerable deafness and tinnitus. This may be due to the obstruction of the meatus or to a coincident tympanic catarrh which may even go on to perforation of the drum. Fever may be present if pyogenic infection occurs which not infrequently happens. This causes the secretion to become purulent, which with the swelling may cause the condition to be confused with furunculosis of the meatus.

Local treatment is necessary along with the constitutional. The part should be kept clean by daily cleansing with a weak bichloride solution. Applications of lotio nigra—black wash—on pledgets of cotton, or dusting with calomel should be used in the interval.

Myringitis.—In rare instances condyloma of the drum has been observed. Myringitis, inflammation of the drum may occur secondary to condyloma of the meatus or from eruptions on the tympanum. When thus occurring it will be acute. Not infre-

quently this acute inflammation does not entirely subside and the condition becomes chronic. In this event there may be perforation of the membrana tympani or excessive thickening of the same causing impairment of hearing which is rarely, if ever, restored to normal.

Middle Ear.—In the secondary stage the middle ear is not infrequently affected by an extension from the pharynx or nasopharynx of moist papules—mucous patches—which may cause perforation of the drum and later give rise to an obstinate middle ear suppuration by reason of a pyogenic infection added thereto. I am in accord with Gradenigo and with Gerber that acute otitis media occurring in early syphilis is almost invariably due to an extension of a papular eruption thereon. I believe also with Glogau that not infrequently in syphilitic angina, symptoms of tinnitus impairment of hearing and otalgia may be present without the middle ear being directly involved. The contingency of acute otitis media should always be borne in mind when these patches are present in the nose or throat. Acute middle ear disease does not always come from an extension of these patches. Sudden deafness which cannot be relieved by mechanical treatment and in which shortened bone conduction is present is frequently due to labyrinthitis. This form of deafness, affecting almost invariably both ears is peculiarly characteristic of syphilis. There is rapid destruction of the membrana tympani and the loss of bone conduction is pronounced. Pain is usually present and as in other syphilitic affections is usually worse at night. Tinnitus is present, also vertigo which may be very marked, vomiting sometimes occurs, and prolonged nystagmus. These last symptoms are indicative of a state of irritability of the static labyrinth.

It must be admitted that the diagnosis of these cases in so far as their being due to syphilis is concerned is not always easy even to aurists of experience, because of the fact that syphilitic middle ear disease presents no pathognomonic characteristics, and the presence of syphilis by no means precludes ear infections due to other causes. In a general way however it may be stated that those cases which do not clear up under ordinary treatment and which come on suddenly should always arouse a suspicion of syphilis.

Tertiary Syphilis of Ear.—Tertiary syphilis may attack the external ear in the form of gumma and unless promptly recognized and controlled may cause extensive loss of tissue and consequent disfigurement. Garzia was of the opinion that many cases of prolonged middle ear suppurations are due to syphilis. With his opinion I am in accord. In tertiary syphilis the bony structures of the middle and inner ear are involved and the deafness resulting from the destruction of the delicate bony framework including the

ossicles is usually beyond recall. In some instances gummatous ostitis of the temporal bone composing the ear when deep seated may give rise to hemorrhage owing to ulcerative erosion of the lateral sinus or the internal carotid artery. Gumma of the temporal bone in proximity to the ear may however occur without involvement of the auditory apparatus.

Prognosis.—The prognosis of these cases is not good in so far as restoring the hearing is concerned. If seen at the beginning it is possible in quite a few instances to restore the hearing in part at least; that is the patient can be prevented from becoming totally deaf. Should a gumma of the mastoid become infected and a pyogenic meningitis threaten, relief by surgical interference is necessary. Similar procedure is required for the removal of sequestra that may form. Intensive treatment by arsphenamine, mercury and potassium iodide must of course be used in conjunction with any mechanical measures.

Labyrinthitis.—Tertiary labyrinthitis differs somewhat from that occurring in the secondary stage. The loss of hearing is gradual owing to the fact that while high notes may be lost and bone conduction entirely abolished or at least very much impaired, aïr conduction may be fairly well preserved. In very many cases the defect is only discovered when searched for. Vertigo may be present and it may be the only symptom the patient complains of; but it is just as often absent. Tertiary labyrinthis is frequently diagnosed whereas the process in reality involves the auditory nerve. Approximately 7 per cent of deafness occurring in the tertiary stage of syphilis is labyrinthine, but deafness occurring in the tertiary stage due to involvement of the auditory nerve is five times as great. That is for every case of labyrinthine deafness there are five which are due to involvement of the nerve. From carefully gathered statistics, Beck found that in 80 per cent of syphilitics whether suffering from auditory lesions or not, there was more less impairment of bone conduction, although in many instances there was no impairment of hearing. He attributed this to increased intracranial pressure such as obtains in brain tumor or hydrocephalus. He found further that when some of these patients had a lumbar puncture the impairment of bone conduction disappeared for a time but always returned. While he does not so state we now know the reason for this in the comparatively frequent invasion of the nervous system by the Treponema pallidum as evidenced in the pathologic changes observed in the cerebrospinal fluid in a large percentage of syphilitics. This also explains why deafness due to nerve lesions is so much more frequent than deafness due to syphilitic disease of the osseous or membranous structures which compose the auditory apparatus. I am therefore in full accord with Swift and Ellis that

rapidly progressing or sudden deafness occurring usually in tertiary syphilis—although it may occur in the secondary stage of the disease—is generally significant of involvement of the central nervous system. The frequency of syphilitic nerve deafness has also been commented upon by Benario and by Habermann and by Mayer. The earliest onset of a lesion of the eighth nerve, the symptoms appearing one week following the development of the chancre, was reported by Politzer in 1908. Three years previously Rozier reported 2 cases of auditory nerve involvement occurring a few days before the appearance of the secondary eruption. In 1905 Gradenigo expressed the opinion based upon an extensive series of investigations that the nerve stem rather than the labyrinth was involved in the majority of cases of syphilitic deafness. However, he admitted that "the clinical differentiation of nerve stem and labyrinthine disease is one of the most difficult tasks of the otologist." Rosenstein also considered labyrinthine involvement comparatively rare as compared with nerve involvement. Nonne later pointed out the frequency of disturbance of the acoustic nerve in association with disturbance of the other cranial nerves. His conclusion was that most of these auditory disturbances were due to an involvement of the nerve in a basal meningitis. Knick and Zaloziecki expressed a similar opinion.

This involvement of the auditory nerve expressed by sudden deafness or a deafness that gradually increases without any changes observable in the auditory apparatus is of special significance if we realize that it is in many instances the first clinical indication of involvement of the central nervous system; since it often appears before the classical objective signs of the Argyll-Robertson pupils, loss of the ankle and knee reflexes, and, if paresis is developing before any mental changes are observed.

Auditory Nerve Involvement.—When the eighth nerve is involved it is impossible with our present knowledge to definitely locate the lesion. By that I mean that we cannot say whether it is the spiral ganglion, the nerve trunk or the roots and nuclei. Functional tests are of no avail. It is a remarkable fact that in many of these cases of involvement of the auditory nerve hearing may be well preserved and there may be no complaint of vertigo even when the vestibular nerve or the semicircular canals are involved. Not infrequently hyperacusis or increased acuity of hearing is the first manifestation of involvement of the nerve. Since the involvement of the nerve is due to a basal meningitis it is to be supposed that other of the cranial nerves are also attacked. This is true, and of these the facial in particular is most often involved. But, as has been observed by Moos and Steinbrugge there may be considerable degeneration of the facial nerve without any signs whatsoever.

Formerly the prognosis of these cases was very poor, not only as to the deafness but also as to the progress toward tabes or paresis of which the involvement of the nerve of hearing is rightly considered a harbinger. Now however, if diagnosed and treated intensively before the process passes beyond control many of these cases can be arrested and not a few of them cured. For the management of these cases the reader is referred to the chapter on Treatment.

Congenital Syphilis and Deafness.—Congenital syphilis is a most frequent cause of deafness. It is one of the triad of Hutchinson; the other two being interstitial keratitis and notched upper central incisors. As syphilis often attacks the visual apparatus *in utero* so does it attack the auditory apparatus. Gruenberg has demonstrated the Treponema pallidum in microscopic sections of the cochlear and vestibular nerves and in the carotid and tympanic plexuses and about the vessels of the middle ear and in the marrow of the ossicles of a seven months' syphilitic fetus. In a dead-born syphilitic fetus Fraser observed bilateral otitis media, abnormal spacing between the auditory cartilages and bones and small cell infiltration of the auditory nerve and labyrinth. Very few infants in whom these profound changes occur survive. If they do, it is as congenital deaf mutes. In quite a number of cases of so-called congenital deaf-mutism aural syphilis occurs before the infant has learned to talk, but it was not present at birth. This happens most frequently in those cases in which "snuffles" develop shortly after birth and is due to an extension through the Eustachian canal which in turn is secondary to the lesions in the nasopharynx. The middle ear is involved and also the labyrinth. In many of these cases there is middle ear suppuration which in quite a few instances also involves the labyrinth.

Congenital Syphilis of the Eighth Nerve.—Congenital syphilis may cause a degenerative inflammation of the acoustic nerve. This is as a rule primary but it may also be secondary to a periostitis of the auditory osseous structures; it may also be secondary to a basal meningitis. I might add in passing that in many of those cases in which the process originates by extension from a basal meningitis, symptoms of bulbar involvement as evidenced by crossed paralyses of the Brown-Sequard type, are observed. In congenital syphilis of the eighth nerve the nerve may be involved alone, or the involvement may include the nerve supply of the vestibule and cochlea, or the labyrinth may also be included. Again, the static labyrinth may not suffer. The deafness in these cases may come on with startling suddenness or it may come on gradually. Or, deafness may not be present but tinnitus and vertigo may be the only symptoms present without impairment of hearing.

Lesions of the auditory nerve in congenital syphilis rarely occur

before the third or fourth year—usually between the tenth and fourteenth years. Females are much more frequently affected than males. In not a few instances coincident with the aural lesion, keratitis develops. As in acquired syphilis most of these congenital syphilitic aural lesions are bilateral and this tendency to affect both ears is so characteristic that in a sense it may be regarded almost as pathognomonic of syphilis.

Syphilis Hereditaria Tarda.—Aural lesions due to *syphilis hereditaria tarda* are not infrequent. It may be the only late manifestation of the congenital diathesis. It almost invariably shows itself as a labyrinthitis, and in its symptomatology it nowise differs from that seen in the acquired disease. This, and the fact that it usually occurs in young adults between twenty and thirty years of age, often causes difficulty in differentiation as to whether it is congenital or acquired. Congenital syphilitic labyrinthitis usually begins suddenly and is not attended with pain. It progresses rapidly and there is early loss of bone conduction. There is special loss of hearing for high tones. This loss of perception for high tones is so characteristic that many aurists regard it as a pathognomonic symptom. Tinnitus may be present. When occurring in children however, this symptom is usually absent. As a rule vertigo does not occur. A mild tympanic catarrh is often present but its presence has no bearing whatsoever on the disease. Labyrinthitis due to *syphilis hereditaria tarda* occurring after twenty years of age rarely causes deaf mutism. The voice becomes flat and toneless and enunciation of vowel sounds is apt to become indistinct.

Prognosis.—The prognosis of congenital aural syphilis is not good. If the sense of hearing is not entirely lost it is almost invariably seriously impaired. In a few instances perhaps, in which the diagnosis has been promptly made and vigorous treatment instituted, or where the process has been mild and of a non-destructive character, there may be no impairment of hearing. In not a few cases when the deafness occurs before the tenth year of life, the mental status, which at best is rarely good, deteriorates, because of the isolation created by the loss of the faculty of hearing.

Neurorecidive Lesions and Arsphenamine.—I shall close this chapter with a brief discussion of the so-called neurorecidive lesions of the eighth nerve occuring after the injection of arsphenamine. It has been asserted by some, notably by Alexander and Bruehl, that neurorecidive lesions, especially of the eighth nerve have been of much more frequent occurrence since the advent of arsphenamine. These relapses they and other ascribe to the use of this drug. This has been denied by Ehrlich, also by Benario and Frey, and with them I am in accord. I do not believe that relapses of lesions of the eighth nerve in particular or of nervous lesions in general are more fre-

quent now that arsphenamine has come into common use than when such lesions were treated exclusively with mercury and potassium iodide. Nor do I believe, as has been also stated, that syphilitic nervous lesions are more frequently encountered since the advent of arsphenamine than they were previously. If there is a seeming increase in nervous syphilis, which I am willing to admit, I believe it is due partly to an evolution of the disease (the discussion of which would take us too far afield), but it is due more to the fact that nervous syphilis is diagnosed with greater accuracy than heretofore. It is possible that nervous syphilis and recurrences of the same are more prevalent under the sway of arsphenamine than under that of mercury and potassium iodide, because, as Nichols suggests, arsphenamine destroys such large numbers of the Treponema pallidum and does so with so much more rapidity than mercury, that antibodies do not have time to develop, and consequently any focus remaining in the nervous system can develop without let or hindrance. The only way to prevent neurorecidive occurrences—if such there be—is to give arsphenamine intensively and to follow its use with a similar intensive course of mercury and potassium iodide. If this were invariably done I am convinced that we would hear less of neurorecidive syphilis.

CHAPTER XLV.

SYPHILIS OF THE NOSE AND THROAT.

The earliest observers of syphilis were aware that the disease attacked the nose and throat with comparative frequency. The physicians of India and China two thousand years ago described with surprising accuracy syphilitic lesions of these parts. At a much later period during the recrudescence of the disease in the early sixteenth century the writers of the time looked upon ulceration of the larynx, and pharynx, and necrosis of the nasal bones as especially significant of the infection. Fracastor in his famous poem alludes to the change in the voice due to ulceration of the larynx and Petronius in his work, *De Morbo Gallico*, published in 1566, lays stress on the chronic hoarseness—*vox rauca perseverans*—so often present in those afflicted with syphilis. Nearly one hundred years later Severinus cited and described cases of syphilitic ulceration of the trachea and epiglottis. In the eighteenth century syphilis of the nose and throat was described in detail by Boerhaave, Anstruc, Plenck, Bell, and Swediaur. In the early years of the nineteenth century Thomann made some valuable contributions to our knowledge of syphilis of the trachea and a few years later Altenhofer called attention to the fact that tracheal phthisis frequently followed syphilitic disease of the trachea.

While deformities such as complete destruction of the nose and of the hard and soft palate whereby the nasopharynx and buccal cavity are converted into one, are now rarely seen, yet the variety of lesions which syphilis especially in the tertiary stage can give rise to in these organs requires consideration. To the rhinologist and laryngologist they are of momentuous importance.

SYPHILIS OF THE NOSE.

Chancre of the Nose.—Chancre of the nose is an extremely rare form of extra-genital infection. It probably occurs from picking the nose with a contaminated finger. In appearance the lesion does not differ from those occurring elsewhere. It is usually found just within the nostril or on the septum; when on the septum it sometimes causes perforation; as a rule however, even if large, it heals without leaving an appreciable scar. The submaxillary glands on

the same side as the lesion are invariably enlarged as are also the preauricular glands. If the chancre is on the septum the pharyngeal glands will be enlarged as well. Unlike chancres occurring elsewhere, chancre of the nose is frequently attended with neuralgic pains of considerable severity. These pains are on the same side of the face as the chancre and are usually most intense about the eye. Nasal chancre is sometimes confused with epithelioma but there should be no difficulty in making a diagnosis. Epithelioma is rarely observed in those under middle age, although it must be remembered that an extra-genital chancre can occur at any age. A chancre, even without treatment of any kind will nearly always heal within five or six weeks—it is extraordinarily rare for it to remain unhealed longer than two months; whereas epithelioma does not heal within that time. Also, it is frequently possible to detect the Treponema pallidum in a drop of serum expressed from the chancre. After the lesion has existed for three or four weeks a positive Wassermann reaction of the blood may be obtained; before that time the Wassermann reaction may be negative. The therapeutic test will also clear the diagnosis.

Secondary Syphilis of the Nose.—In the secondary stage the generalized erythema is sometimes seen on the nasal mucous membrane; less frequently however than on the mucous membrane of the larynx and the pharynx. These lesions may give rise to a slight—very slight—nasal catarrh, which passes away as soon as constitutional treatment is begun. In some instances mucous patches occur on the nasal mucous membrane under which circumstances the discharges from the nose may be slightly tinged with blood and if the ulceration is in any way severe epistaxis of a moderate degree may occur due to erosion of some small vessel. In rare instances condylomata have been known to occur at the mucocutaneous junction of the nostrils and the upper lip. In common with all secondary eruptive lesions those of the nose and throat are never destructive and, when they disappear, they leave no trace of their former presence.

Tertiary Syphilis of the Nose.—Tertiary lesions are of much more serious import. Not that they are dangerous to life but because of the deformity and disarrangement of the anatomic relations of the nose that they may cause. It is also to be noted that they are often—too often I may say—unrecognized before irreparable damage has been done. The mucous membrane, the bones, the cartilage and the nerves which together form the nasal structure, alone or together may be attacked by tertiary syphilis. The destructive ulceration of this stage may be the only manifestation of the disease and since it may occur after a lapse of many years, perhaps after all remembrance of the initial infection has been forgotten, and also

because it may very closely simulate tuberculosis or malignancy, it can be readily appreciated that clinical diagnosis is not always easy.

Gumma of the Nose.—Gumma or gummatous infiltration are the characteristic pathologic processes of this stage. Gumma of the nose usually occurs on the floor of the nostril or on the cartilaginous portion of the septum. It may also occur on the inferior turbinate, the nasal bones or the mucous or cutaneous surfaces of the alæ of the nostrils. It usually originates in the submucous tissue, although it may begin as a perichondritis or periostitis. A nasal gumma begins as a deeply red, more or less circumscribed tumor that is firm to the touch of a probe and does not shrink when a solution of cocaine is applied. It may have attained considerable size before the patient is aware of it. The patient then complains of a sense of fullness in the nose and the nasal secretions are increased. Because of the nasal obstruction there is often headache. The cutaneous surface of the nose is often slightly reddened and edematous and the nose feels tender when touched. If the obstruction is marked there may be a nasal tone to the voice. If recognized at this stage the neoplasm rapidly resolves under treatment and little if any damage results therefrom. If not recognized the gumma sooner or later breaks down and when this happens the pains are generally relieved. The discharge of the gummatous detritus is thick and blood stained and of an offensive odor. Scabs and crusts of a brownish or yellowish color form which when removed may cause epistaxis. The sense of smell is much impaired and in some instances it is entirely lost. Should the process be allowed to continue unchecked it will ultimately involve the bone beneath, and necrosis will occur. Pyogenic infection is soon grafted upon the already existing syphilitic infection and hastens and augments the osseous necrosis which rapidly becomes evident by the particularly foul and offensive odor imparted to the discharges from the nose and also by the bony sequestra which from time to time come away. It is these cases which lead to "saddle nose" and destruction of the septum involving both the osseous and the cartilaginous portions.

When instead of a circumscribed gumma there is gummatous infiltration of the nasal mucous membrane the signs and symptoms are rather more obscure and hence the difficulty of clinical diagnosis is increased. The symptoms partake at first of a chronic rhinitis which may affect one nostril only. There is a feeling of nasal obstruction and the sense of smell is impaired; a slight discharge is present. The nose may be slightly reddened and tender and the tenderness is more diffuse than it is when the gummatous process is circumscribed. The mucous membrane is congested and the vestibular openings of the nose may be occluded, either one or both,

according as the disease affects one or both sides of the nose. Gummatous infiltration of the nasal mucous membrane may extend to the bone and involve the same, in which case the end-results are identical with those caused by a circumscribed gumma; or it may cause a destructive perichondritis and perforate the cartilaginous septum or destroy the cartilaginous alæ and thus cause a collapse of the nostrils giving rise to the deformity known as "sheep nose." In some instances the syphilitic necrosis may extend to the lacrimal, ethmoid or sphenoid bones and if the meningeal coverings of the brain are exposed in consequence a fatal meningitis may result. It is needless to say however, that such complications are now extremely rare.

Sequelæ of Gumma of the Nose.—Following the extensive destruction of the ciliated epithelium and cavernous erectile tissue due to gummatous infiltration the condition known as atrophic rhinitis frequently supervenes. The mucous membrane is dry and glazed and there is more or less complete atrophy of the middle and lower turbinates. The nasal fossæ are thereby much more spacious than they otherwise would be. The shrunken mucous membrane is covered with tenacious, foul smelling muco-pus which unless frequently removed forms dry, yellowish scabs or crusts. The olfactory sense is entirely lost, and the dilated nasal canals causes an intractable dryness of the pharynx and larynx—a condition which renders these parts especially susceptible to infection with the tubercle bacilli.

Gummatous infiltration sometimes causes the lower and middle turbinates to enlarge and undergo fibrous transformation in which event they present as hard, yellowish projections in the nasal passages which may cause considerable obstruction and disarrangement of the anatomic relations of the parts. This condition frequently is concomitant with atrophic rhinitis, although not always.

Diagnosis of Tertiary Syphilis of the Nose.—The diagnosis of tertiary lesions of the nose is usually not difficult. Unfortunately in many instances in the beginning the slight and obscure symptoms, resembling as they do a benign nasal catarrh, are allowed to continue unchecked or else are treated by measures totally inappropriate considering the cause of the condition, so that ulceration and destruction have taken place before the patient is sufficiently alarmed to go to a physician. In cases where necrotic bone exists it is well to remember that necrosis of the bones of the nose is hardly if ever the result of any other cause than syphilis. While the odor from necrosis of the nasal bones may suggest ozena it must be born in mind that the odor of ozena is entirely different from that of syphilitic necrosis—the odor of ozena is said to resemble crushed

bedbugs—whatever that may be like—there is no ulceration of the nasal mucosa and there is no caries of the nasal bones. The ulceration of lupus is of much slower progress, there is no characteristic odor and there is no destruction of bone. An ulcerating gumma may be mistaken for malignant disease but an examination of the tissue and the Wassermann reaction or the therapeutic test will enable a differential diagnosis to be made. Also, in malignant disease the tendency to hemorrhage from the nose is much greater than with gumma, and the pain is much more acute.

Perforation of Septum.—Perforation of the cartilaginous nasal septum can be due to other causes than syphilis. It is only where the bony portion of the septum is perforated that syphilis should be strongly suspected. There may be congenital absence of the cartilaginous septum or it may have been perforated as the result of a surgical operation for deflected septum that was not altogether a success. It may be perforated by reason of ulceration due to typhoid fever, variola or a furuncle. It is not infrequently observed in workers in chrome and allied substances due to the ulceration caused by the irritating fumes.

If recognized in time these lesions can be made to heal by constitutional treatment in an amazingly short space of time. If external deformity has occurred the contour of the nose can often in a measure be restored by a plastic operation or by the injection of paraffine. Stenosis of the nostrils may require the permanent use of rubber or silver tubes. Hypertrophy of the turbinates requires surgical removal. Sequestra of dead bone should be removed, but this removal should not be attempted until complete separation from the healthy bone has taken place. Atrophic rhinitis cannot be cured and the status of the condition is not influenced by constitutional treatment. The nasal fossæ should be kept as free as possible of crusts and mucopurulent discharges by the frequent use of alkaline solutions with a nasal douche after which albolene combined with oil of eucalyptus or camphorated oil should be sprayed into the nose.

"Snuffles."—The most frequent and characteristic nasal lesion of early congenital syphilis is "snuffles;" I wish to say however that every infant with "snuffles" is not necessarily syphilitic. It is one of the earliest signs of the disease and not infrequently occurs before the appearance of the rash. The mother usually thinks the infant has a "cold" and it is often wise not to change her opinion. The snuffling of the infant is due to an edema of the nasal mucous membrane which is also slightly ulcerated. An acrid discharge may be present but this is not always so. If congenital syphilis is promptly recognized and treated no ill results follow this inflammation, but if it is not diagnosed the nasal bones become involved and the "saddle nose" deformity one of the pathognomonic

stigmata of congenital syphilis, follows. When the nasal bones are involved in congenital syphilis there is invariably an offensive mucopurulent discharge, and in infants or young children in whom this is present congenital syphilis should always be suspected.

SYPHILIS OF THE PHARYNX.

Primary Lesion of Pharynx.—The pharynx may be attacked by syphilis in the primary, secondary or tertiary stages. Chancres are necessarily rare in this location. Formerly they sometimes occurred from the use of contaminated instruments but such accidents are now of very rare occurrence. The most frequent site for pharyngeal chancre is the tonsil. The chapter on Extra-genital Chancre contains a description of this type of extra-genital lesion.

Secondary Syphilis of the Pharynx.—In early secondary syphilis pharyngitis is a very frequent symptom. This pharyngitis is due to the presence of mucous patches and is usually very painful, especially on swallowing. In some instances however, the patches may be numerous and large and yet the pain experienced by the patient is very slight. In not a few instances the pharyngitis of the early secondary stage is nothing more than an erythema and is attended only with a slight dryness. Even this may not be present and despite a marked macular or papular eruption the pharynx may entirely escape. As a rule, however, this does not occur and if the eruption is severe there is nearly always a severe pharyngitis. The pharyngeal inflammation of the secondary stage is invariably superficial and transitory and soon passes away when treatment is begun.

Tertiary Syphilis of the Pharynx.—Tertiary syphilis attacks the pharynx either as a gumma or as a gummatous infiltration. As with the nose it is not infrequently the sole manifestation of tertiarism. These late lesions of the pharynx are sometimes difficult to diagnose, but early diagnosis is all the more important because of the disastrous consequences that sometimes follow with startling rapidity when they have become fully established. A gumma of the soft palate that the patient was hardly aware of may over night perforate into the nasal cavity and cause a deformity that art cannot overcome.

Gumma of the Pharynx.—Gummatous disease of the pharynx may occur on the hard or soft palate or the lateral or posterior walls or it may involve a tonsil. On the hard palate it usually begins in the submucous tissue, although in some instances it may begin in the bone itself. Gumma of the hard palate begins as a circumscribed red swelling usually in the midline posterior to the incisor teeth.

It develops slowly and may cause no symptoms whatsoever. When it breaks down—and it is often at this time that the patient first becomes aware of it—it forms a round, dirty looking ulcer at the bottom of which is a floor of bone in a more or less advanced stage of necrosis. Gumma of the soft palate also occurs in the middle line and if seen before perforation takes place it appears as a red, circumscribed bulging of the soft palate. Since it may interfere with the movements of the palate a gumma in this locality is more frequently recognized before destructive ulceration occurs than when it occurs on the hard palate. The perforation may be large or small or the entire soft palate may be destroyed. Gumma of the posterior wall of the pharynx if above the level of the soft palate may go on to ulceration without being discovered. If allowed to continue the gummatous ulceration may penetrate to the vertebræ.

When the gummatous disease is an infiltrate rather than a circumscribed neoplasm it may involve the entire pharyngeal vault or, more frequently, the lateral walls and the tonsils. With gummatous infiltration there is less tendency to break down and form ulcers.

As I have already stated the disease may be far advanced before it is recognized. Pain is usually absent even when severe destructive ulceration is present. Pain may be present however, and it usually radiates toward the ears. In some cases there is dysphagia and difficulty in clearing the throat of mucus. These two symptoms are sometimes sufficiently marked to cause the patient much distress. If perforation has taken place the character of the voice undergoes a decided change which is so characteristic that to the practised ear pharyngeal perforation can be readily inferred. Regurgitation of fluids through the nose occurs, and in some instances it has been the first indication to the patient that the pharynx had been perforated.

Diagnosis of Syphilis of the Pharynx.—There are a number of conditions with which gummatous disease of the pharynx may be confused. It should not be difficult however, to distinguish between them if certain features pertaining to each of them are borne in mind. In the first place it should be remembered that ulceration of the pharynx is in the majority of instances syphilitic. For that reason the Wassermann reaction and the therapeutic test should be thought of first, in order that syphilis may be promptly confirmed or denied. Aside from this, from a clinical standpoint syphilis of the pharynx may be mistaken for malignant disease. In this instance, the age of the patient should be considered—malignancy occurs most frequently in patients over fifty years of age—although it must also be remembered that there is no age limit to the appearance of the lesions of tertiary syphilis. Malignant disease is attended with

intense pain; while there may be pain in syphilitic disease it is never as atrocious as that of malignant disease. In malignancy there is very early involvement of the glandular elements; there is little or no glandular involvement in syphilis. Lupus is sometimes encountered in the pharynx; but its presence in this situation is extremely rare. When it so happens it is nearly always present elsewhere. The ulceration of lupus is extremely slow; it never perforates the pharyngeal walls; there is less infiltration, and the edges of the ulceration are not as sharply defined as the ulceration of syphilis. Tuberculosis of the pharynx can be diagnosed from syphilis by the intense pain, the shallowness of the ulceration and by the fact that it almost invariably occurs in those far advanced in pulmonary tuberculosis. Actinomycosis closely resembles gummatous ulceration and clinically it is sometimes impossible to distinguish between them. The presence or absence of the ray fungus will establish the diagnosis. Glanders may simulate syphilis but the history of the acute attack, the cellulitis of the face, the presence of abscesses in other parts of the body and the finding of the *Bacillus mallei* in the discharges enables a differential diagnosis to be made.

Treatment of Syphilis of the Pharynx.—If promptly recognized syphilis of the pharynx can be cured as readily as manifestations of the disease located elsewhere. Gummata that have not broken down may heal without leaving any trace, but if perforation has taken place a plastic operation or the presence of an obturator in the opening may be necessary. Cicatricial bands or synechiæ may also require surgical interference to overcome the distortion caused thereby, as this cicatricial tissue will not resolve under constitutional treatment.

SYPHILIS OF THE LARYNX.

Chancre of the Larynx.—Chancre has been known to occur in the larynx but it is of necessity most rare—so rare that it need not be discussed here.

Secondary Syphilis of the Larynx.—In the secondary stage of the disease mucous patches frequently occur but, as when they occur elsewhere, they yield readily to constitutional treatment. In the early secondary stage the larynx is frequently congested due to an erythema of the mucous membrane. It is this edema of the mucous membrane that gives the transitory huskiness to the voice so often noted in early syphilis. Condylomata have been observed in the secondary stage but they are for the most part extremely rare.

Tertiary Syphilis of the Larynx.—The lesions of the tertiary stage—gummata and gummatous infiltration—are those which deserve more than passing notice in considering syphilitic disease of the

larynx. The symptoms of tertiary laryngeal syphilis vary within wide limits according to the extent and location of the lesions.

While syphilis of the larynx is not as frequently encountered as syphilis of the pharynx, yet it is sufficiently common—in men more so than in women—and sufficiently important, in that it is frequently the concomitant or precursor of tuberculous or malignant disease, that a knowledge of the lesions met with in this manifestation of syphilis is necessary not only to the laryngologist and syphilologist but also to the general practitioner, to whom these patients usually first present themselves.

Examination of the Larynx.—It may not be out of place here to briefly describe the method of examination of the larynx for the benefit of those who, upon occasion may be called upon to make such an examination. Whenever possible examination of the larynx should be made on an empty stomach in order to avoid vomiting. The retching, which in some patients begins as soon as the mirror is introduced, can however, be prevented by spraying the throat with a 1 per cent solution of novocaine. In fact, I would suggest this precautionary measure in every instance as it always allows a calmer and therefore more satisfactory examination to be made. Before introducing the mirror it should be heated or else covered with a film of green soap as otherwise it will invariably become clouded, and thus prevent a satisfactory reflection. The patient should protrude the tongue as far as possible and the examiner should grasp it with a towel or a piece of gauze. If the tongue bulges upward and thus obscures the view, instead of grasping it with the fingers as already mentioned a tongue depressor may be used. The largest sized mirror should be used as the reflection thereon is proportionate to the actual size of the parts. The mirror should be held gently but firmly against the uvula. If the patient chokes before the mirror is in place tell him to say 'A' as it in "fate." It is incorrect to have the patient say 'Ah' as the epiglottis is only raised in high pitched notes. The reflector should be placed in front of one eye—it is immaterial which—but both eyes should be used in determining the reflected picture.

Symptoms of Tertiary Syphilis of the Larynx.—In tertiary syphilis of the larynx in not a few instances the only symptom is a chronic huskiness or hoarseness of the voice. This hoarseness is not attended with any pain upon using the voice and is due to a gummatous infiltration of the vocal cords whereby they are thickened and their vibratory movements diminished in consequence. Except for this hoarseness the patient may be in otherwise perfect health and the hoarseness is the symptom that causes the patient to consult the physician. In some instances the hoarseness may be associated with more or less dyspnea which is due to the infiltrate encroaching upon

the glottic space and to fixation of the vocal cords. In such an event the patient usually consults the physician for "asthma." This dyspnea may sometimes occur suddenly from edema caused by a sudden change of temperature such as being exposed to the cold and then coming into a warm room. It may also occur from the sudden separation of a necrotic cartilage of the epiglottis.

Gumma of the Larynx.—Gumma of the larynx is not as frequent as gummatous infiltration. The lesion is rarely recognized or indeed, sought for until it breaks down and ulcerates. These new growths may be found on the epiglottis, the aryepiglottic folds, the arytenoid cartilages and rarely on the vocal cords. If by any chance they are looked for and found before ulceration has taken place they do not differ in appearance from a gumma appearing elsewhere on a mucous surface; that is, as a circumscribed dark red tumor elevating the mucous membrane. When ulceration takes place a punched out crateriform ulcer forms, similar in appearance to a gumma of a mucous surface elsewhere.

The cartilages and the hyoid bone are sometimes primarily affected by the tertiary process but usually these structures are affected secondarily by extension of a gumma or gummatous infiltration. This perichondritis may cause the cartilages to necrose and in this event they may be coughed up or they may be expelled through a sinus leading to the cutaneous surface. Gummatous infiltration or gumma of the epiglottis does not always end in ulceration, but not infrequently, especially in gummatous infiltration, the inflammation subsides and the infiltrate is transformed into fibroid tissue which binds down and ankyloses the opposing edges of the cartilages. Should this fibrous shrinkage continue there is grave danger of stenosis of the glottis as the ultimate result. In some instances gummatous ulceration may entirely destroy the epiglottis and this destruction may be attended with absolutely no pain. As a rule however, ulceration of the epiglottis is characterized by dysphagia or pain and difficulty on swallowing.

Paralysis of the vocal cords may be caused by a peripheral neuritis or may be more remote by involvement of the bulbar nucleus. It can also be due to involvement of the recurrent laryngeal nerve. If this paralysis is bilateral the voice will be lost and there will be inspiratory stridor

The general symptoms of syphilitic disease of the larynx can hardly be said to be characteristic and none of them is pathognomic. They may all be simulated by processes not syphilitic. Any persistent change in the voice, accompanied or not with dysphagia or dyspnea with stridor—inspiratory or expiratory—in a person who may appear otherwise in good health should always cause syphilis of the larynx to be suspected.

Syphilis and Tuberculosis of the Larynx.—Tertiary syphilitic lesions of the larynx are to be diagnosed from tuberculosis and malignancy. Tuberculosis of the larynx is usually concomitant with tuberculosis of the lungs. The ulceration of tuberculosis is shallower and more ragged at the edges. It is almost invariably intensely painful; whereas syphilitic ulceration is not painful at all or is only slightly so. In tuberculosis the dysphagia may be so great that the patient can only eat after the throat has been sprayed with cocaine. In syphilis this is never observed. In syphilis the voice may be hoarse and raucous, but it is not weak and the use of it is not painful; whereas in tuberculosis the voice sinks to a whisper and its use is a painful effort.

Tuberculosis undoubtedly frequently follows syphilis of the larynx and for that reason a positive Wassermann reaction is not an absolute indication that the laryngeal lesions are syphilitic. In such cases if the clinical signs are indeterminate resort must be had to the therapeutic test. If the ulcerations heal under the influence of arsphenamine and mercury the diagnosis is perforce, absolutely established.

Malignant Disease of the Larynx.—Malignant disease is more apt to occur in elderly persons and therefore in a patient below the so-called cancer age which may be said to begin at fifty years of age, suspicious lesions of the larynx are more apt to be syphilitic than malignant. However, laryngeal syphilis predisposes to malignancy and under such circumstances the malignant transformation occurs earlier than if it were primary. For that reason even in the presence of a positive Wassermann reaction malignancy cannot in all instances be absolutely ruled out unless absolutely disproved by biopsy or the therapeutic test.

Dysphonia and dysphagia in the absence of demonstrable laryngeal disease may be due to pressure from an enlarged thyroid gland, aneurysm of the thoracic aorta or the innominate or subclavian arteries, or to a mediastinal tumor or enlarged bronchial glands.

While in the active stage syphilitic laryngeal lesions respond promptly to treatment. If cicatrization has occurred however, the sequelæ resulting therefrom—stenosis and distortion of the parts—are not amenable to constitutional treatment. Tracheotomy or intubation may be necessary in some instances of this kind.

Congential Syphilis of Larynx.—In congenital syphilis, catarrhal laryngitis sometimes occurs and the hoarse, croaking cry so often noted in syphilitic infants is undoubtedly caused by it. This form of congenital syphilitic laryngitis presents no essential diagnostic features except that the hoarseness persists for many months. Gummatous disease of the larynx in congen tal syphilis is very rare. It is usually overlooked not only because examination is difficult

but more especially because the process is never attended with pain. The walls of the larynx or the cartilages forming the epiglottis may be attacked. In some instances instead of gummatous ulcers, papillomatous growths occur. The principal symptom is hoarseness. The presence of long continued hoarseness therefore, even in the absence of other symptoms or stigmata of congenital syphilis in an infant or young child, should arouse the suspicion of the physician. Laryngeal tuberculosis in infants or young children can in nearly every instance be ruled out. In infants it is unknown, and in older children it occurs only with extreme rarity. Gumma or gummatous infiltration of the larynx may occur as a manifestation of *syphilis hereditaria tarda* in which the lesions do not differ from those observed in the tertiary stage of the acquired disease. It is most rare; Hutchinson has described several cases, but I have not encountered one.

CHAPTER XLVI.

SYPHILIS AND THE TEETH.

CONGENITAL syphilis is the most important factor in causing malformations of the teeth. A knowledge of the dental dystrophies caused thereby is a valuable aid in diagnosing the dyscrasia either direct or as confirming other evidence.

The dental abnormalities due to syphilis are seen principally in the second or permanent teeth, since these abnormalities are due entirely to influences affecting the dental sacs at a time when the crowns of the temporary teeth are calcified and beyond risk of damage. The defects seen in the first or milk teeth are in the main due to influences exerted by the disease *in utero*. It is also possible that the proneness to decay observed in the first set of teeth in infants with congenital syphilis may be due in a measure to the mercury taken by the mother during pregnancy. This possibility however, may now be almost completely set aside since arsphenamine has so largely superseded mercury.

Developmental Defects of Teeth Due to Congenital Syphilis.—The defects in the development of the teeth caused by congenital syphilis are extremely characteristic and, in many instances, allow a diagnosis to be made without any other evidence; yet, in a surprisingly large number these changes in the teeth are not seen. I will even go so far as to say that the teeth may be perfect in those who in infancy suffered severely from congenital syphilis. Strange as it may seem some lesions of congenital syphilis are not observed when the teeth are affected and when the teeth are not affected these lesions are usually manifest. Hutchinson long ago noted that in cases in which there was ulceration of the soft palate or nose the teeth were nearly always normal, and many other have since confirmed this. It has been further observed that these cases frequently escape ocular lesions such as keratitis which might be said to be pathognomonic of congenital syphilis. I therefore wish to impress upon the reader's mind this important and curious diagnostic fact expressed in the following aphorism:

If there are evidences of ulceration of the palate or the nose the teeth will be normal and the eyes will be normal; if the teeth are affected keratitis is certain to have occurred or will occur in the future, and the nose and palate will not be affected.

It may also be said that those whose teeth are undamaged do not as a rule show the physiognomy of congenital syphilis—a physiognomy which is so characteristic as to be pathognomonic—and which enables the skilled observer to detect the taint with unerring accuracy. There undoubtedly exists a class of congenital syphilitics in whom clinical recognition of their disease is a matter of great difficulty and this is still further increased by the fact that the serological reaction is often negative, especially in young adults in whom the disease has spent itself as it were. This class is certainly not large and if examined skillfully many supposed to be free would undoubtedly show some somatic evidence, but nevertheless the fact remains that we must be prepared to encounter from time to time congenital syphilis in those who show absolutely no corroborative signs of the disease.

In order to properly understand the *raison d' être* of these malformations caused by congenital syphilis it is necessary for us to have a knowledge of the development of the teeth. This includes their several periods of calcification and eruption; the process of dentification, in that it proceeds from the summit of the dental papillæ and gradually forms the crown, neck and root of the tooth; the synchronous process of dentification and amelification. These processes may be interrupted or influenced at any stage of their development and from the dystrophy resulting thereby the stage when the arrestment took place can be definitely determined. Should however, the teeth during their development escape the morbid influence of the Treponema pallidum they will erupt complete in form and structure although manifold evidences of the disease exist elsewhere. Syphilitic stigmata as manifest in the teeth can therefore only be produced during the process of their development and are essentially the result of an interruption in the process of calcification. Because of this suspended or imperfect calcification irreparable degenerative changes are produced which may show on any part of the tooth from its morsal surface to its gingival margin. If the interference occurs when dentification is about to begin the hypoplasia will show upon the morsal surface; whereas if it occurs later it will appear at a higher level or on the facial, lingual or mesial surfaces. It is thus possible to tell whether the lesions began before or after birth and also, within certain limits, the severity of the infection can be determined by the degree of hypoplasia, in that the hypoplasia may be slight or marked—so marked in rare instances that the teeth do not erupt at all.

Syphilitic hypoplasia of the deciduous teeth does not occur; or, only rarely. The reason for this is that the beginning of dentification for these teeth takes place approximately from the seventeenth to the eighteenth week and a fetus affected at this stage of its development is rarely born alive.

Dental stigmata according to Fournier are present in nearly 50 per cent of congenital syphilitics, and Stein believe that they take first place among the dystrophies caused by congenital syphilis.

The permanent first molars, incisors and canines are the teeth which are most frequently affected by congenital syphilis. This is because the first molars begin dentification during the last months of fetal life and the incisors and canines during the first three or four months after birth. The bicuspids may not be affected because dentification in them has not yet begun. This is also true of the second and third molars because with them dentification does not begin until the child is several years old.

The hypoplastic changes in the four permanent first molars are of extreme importance as diagnostic evidence of congenital syphilis. In childhood and adolescence these teeth for two-thirds of the distance from their morsal surfaces are diminished in diameter and eroded and marked off from the remainder by a circular constriction, giving them a stumpy appearance, or rather that of stumps of dentine emerging from apparently normal crowns. They are grayish, black or yellowish and as the child advances in years the stumps gradually wear away so that they finally show only the crowns with flat, yellow morsal surfaces. Later the central portion of these eroded morsal surfaces may become carious and the teeth are destroyed. Thus the congenitally syphilitic youth may show either a characteristic erosion or a more or less advanced caries of the four first molars.

"Hutchinson's Teeth."—The dental hypoplasia which affects the two upper central incisor teeth and which is characterized in its typical form by a crescentic indentation of their morsal surfaces is known as "Hutchinson's teeth," and except to the teeth named the term is misapplied. But a similar hypoplastic change has also been noted in the four lower incisor teeth and even in the canine teeth. In addition to the crescentic depression Hutchinson's teeth are also "screw driver shaped" and converge obliquely. Hutchinson's teeth when typical have such a characteristic appearance that they can be recognized at a glance. When these teeth first erupt the semilunar indentation upon their morsal surfaces does not exist. The surface where the indentation is to come later is filled with hypoplastic tooth tissue either in the form of acuminate buds or spicules which form a fine denticulation, or in the form of a more or less homogenous lobular mass. This hypoplastic dentine which is not covered with enamel is very friable and therefore rapidly crumbles away, so that in a few years it entirely disappears and in its place we have the crescentic notch which is characteristic of these teeth. During adolescence the morsal surfaces gradually change and in time their characteristic appearance is lost. This is due to

the wearing down of the arcs of the morsal surfaces which finally disappear about the twenty-fifth year and their surfaces are then rectilinear. Even as late as this however, an important characteristic still remains. This is to be observed in the beveling of their inferior facial surfaces, imparting a slant from the facial to the lingual surface. These bevels are the last to go and this occurs at about the thirtieth year. This leaves the teeth short and stumpy and the presence of such teeth along with other dystrophies or the remains of past lesions are strongly suggestive of congenital syphilis. The hypoplastic changes just described are not always limited to the two upper central incisors; they have been observed on the upper lateral and lower incisors and, exceptionally, on the canines. Legros, Hutchinson, Moon, and Fournier report having observed the characteristic notch on one upper incisor, the other being normal.

It is only rarely that the lateral incisors show any peculiarities that may be ascribed to syphilis. The same is true of the lower incisors, canines and molars. All of them however may be dwarfed and foliated, but where these conditions exist in the absence of the characteristic peculiarities of the upper central incisors they are not to be taken as decisive evidence of congenital syphilis as they may be due to other causes.

Other dental abnormalities such as abnormal placement of the teeth, dental amorphism or teeth of irregular shape, absence of certain teeth or supernumerary teeth, may be caused by congenital syphilis and when present should always be looked upon with suspicion. The same is true of teeth which show an excessive liability to decay; also asymmetry of the maxillary bones and palatal deformities.

Congenital syphilis sometimes affects the teeth by causing the appearance of pits and furrows on their surfaces. These depressions may be only slight or they may be of considerable depth. When closely examined the bottoms of these depressions will be found to be irregular and in young teeth may be white but in the course of a few years they become brown or black. They are usually to be seen on the upper central incisors. They may vary in number and are sometimes arranged in a horizontal line; more rarely in two superimposed horizontal lines. The furrows are more frequently met with than the pits, and teeth so affected appear as if they had been transversely scratched. As the teeth become older these scratches become darker. For that reason they are less noticeable in early life than later, and are always more pronounced in males than in females, possibly because of the use of tobacco. Two superimposed furrows may exist which may be separated by a distinct ridge. When present these furrows are

located nearer the morsal surfaces than the gingival margins. Teeth with these pits and furrows are prone to erosion and decay.

Children who in infancy, because of congenital syphilis, have received mercurial treatment, may sometimes show evidences of the stomatitis caused thereby in their permanent teeth. In the teeth of such children there will be seen transverse ridges on the upper and lower incisors and the crowns of the first molars will be eroded. These changes are probably due to an inflammation of the tooth pulp at some period during infancy and are distinct from the arrested development due to the syphilitic dyscrasia.

While syphilis implants a stigma that is infallible upon the teeth so that in the absence of all other signs it can be asserted with absolute certainty that the possessor of such teeth has congenital syphilis; yet, it is equally true that in a very large number the teeth are by no means so characteristic that an opinion can be based upon them alone. There is no question that dental abnormalities should arouse suspicion and they should be allowed proper weight in addition to other corroborative facts but it must be remembered that it is the upper central incisors—Hutchinson's teeth—which alone are pathognomonic of congenital syphilis. Other malformations may be due to syphilis, or, they may be due to other causes, but they are never so pathognomonic that from them alone a diagnosis can be made.

A very common error is to overlook the fact that the milk teeth never show the characteristic changes observed in the permanent teeth. Not infrequently the sacs become inflamed and infected with pyogenic organisms and in consequence the crowns of the teeth are exfoliated before they cut through the gums. The occurrence of this is the strongest evidence in support of the assertion that the gums and tooth sacs are liable to syphilitic inflammation at a very early phase of congenital syphilis. The deciduous teeth are extremely prone to carious degeneration in congenital syphilis. The neck of the tooth is attacked and disintegration is rapid causing the crown to drop off. In this way all of the teeth may be destroyed and the child from the age of two to six years may be without teeth.

Persistence of the Deciduous Teeth.—Microdontism, or persistence of the deciduous teeth is sometimes observed as one of the stigmata of congenital syphilis. This persistence of the deciduous teeth, that is their non-replacement by the second or permanent teeth, occurs more frequently than is usually supposed—in one-third of all dental stigmata according to Champret. Comparatively few physicians or dentists recognize this anomaly, yet it is an important indication of the disease. The deciduous teeth which remain for a longer time than usual are the following in their order of frequency: the second molars, the first molars, the canines, the incisors. The

persistence of these teeth is due to the absence or arrested development of the teeth which should replace them.

Acquired syphilis as it affects the mouth has no effect upon the teeth. It has been stated that in syphilis there is a tendency to tartar formation. I cannot say that I have observed this. If the patient keeps his mouth reasonably clean there is no reason why these deposits should occur any more than they would if syphilis were not present. In tabes and in the later stages of paresis the teeth frequently drop out. This is due more or less to trophic changes and to pyorrhea to which these patients are liable. In the tertiary stage syphilis can cause pyorrhea alveolaris by reason of a periostitis or ostitis of the maxillary bones.

Every patient who has recently acquired syphilis should lose no time in having his teeth attended to. Spongy gums should be treated, tartar removed and cavities filled before treatment with mercury is begun. If these precautions are not taken, mercury, no matter in what form administered, will not be well tolerated.

While mercury is being administered the teeth should be kept scrupulously clean. This includes not only the use of the tooth brush after each meal, but the interstices between the teeth where particles of food are apt to collect, should be kept free of such by means of a thread of dental floss. A potassium chlorate mouth wash should also be used with more or less frequency. Should the teeth become loose and the gums sore from the ingestion of too much mercury the drug should be stopped and potassium iodide given to hasten its elimination. Should there be much salivation atropine should be given. A brisk purge with a saline is of benefit. The gums should be painted with a mixture of equal parts of tincture of aconite and tincture of iodine, and the potassium chlorate mouth wash should be used with more frequency than before.

Syphilis and Dentistry.—The configuration of the teeth which syphilis causes is naturally of interest to the dentist but the dentist should also be interested in the manifestations of buccal syphilis from the very intimate standpoint of prevention of personal infection when working on the teeth of a patient with active syphilis. For that reason whenever syphilis is suspected rubber gloves should be worn. While such a procedure undoubtedly interferes with manual skill the safety which such a precaution provides more than compensates for the diminution in dexterity.

Also, while it is not within the province of the dentist to diagnose syphilitic lesions of the mouth, a general knowledge of the same is well worth his while to know.

Chancre.—Chancre of the lip is of not infrequent occurrence and I have described its physical appearance in the chapter on Extra-

genital Chancre. The gum is sometimes, although rarely the site of chancre. It appears as a circumscribed indolent sore surrounded by an inflamed areola. Chancre of the gum has been mistaken for a malignant growth but the rapid glandular enlargement of the submaxillary glands, its comparative painlessness and the absence of vegetations, and the fact that it shows no tendency to bleed which is characteristic of malignancy helps to make a clinical diagnosis possible.

Mucous patches are perhaps the most frequent syphilitic lesions encountered by the dentist. Their appearance is described elsewhere in this book. It must be remembered however, that herpes of the mucous membrane and glossitis may be easily mistaken for mucous patches. Gumma of the tongue may be mistaken for malignancy but the diagnosis of these lesions is not difficult. The same factors which exclude malignancy in the diagnosis of labial chancre apply here. Leukoplakia lingualis and sclerosis of the tongue are usually indicative of syphilis although not in every instance.

Since the dentist however, is not interested in treating these conditions which are included in the domain of medicine rather than that of dentistry, they are of moment to him, as I have already stated, only as a possible source of infection to himself or others should he by any chance neglect to sterilize his instruments after using them on a syphilitic patient. In the presence therefore of any suspicious lesion in the mouth the dentist should at once realize the ancient adage that "an ounce of prevention is worth a pound of cure" and take the necessary precautions.

CHAPTER XLVII.

THE PROPHYLAXIS OF SYPHILIS.

The contagiousness of syphilis was recognized before it was known to be infectious, and physicians early sought to prevent the disease by advocating prophylactic measures. None of them however, until quite recently, possessed any preventive value; this can be readily appreciated when we consider that these measures consisted chiefly in lotions with which the parts were bathed, the ingredients of which were nearly always of very doubtful value. White wine and vinegar had considerable vogue some four hundred years ago, as did also lime juice which was extolled as a sure preventive of the disease by Fracastor. The great surgeon and anatomist of the sixteenth century, Fallopius found time when not operating on the living or dissecting the dead subject, to concoct what he believed to be a sure preventive of the pox. This sovereign prophylactic was a lotion composed of mercury and guaiac. It was applied immediately after coitus and was followed by a compress soaked in a decoction of aromatic herbs. Lotions of equal parts of the individual's urine and camphor water were also recommended. It is interesting to note that a modification of this method of prevention has persisted to the present day, in that among the ignorant—in this country they are mostly foreigners—there are those who practise washing the parts with their urine in order to prevent venereal disease in general. Hunter advocated a solution of bichloride of mercury and lime water and Ricord believed that Labarraque's solution was an efficient preventive. It is needless to state that all of these have been long relegated to the limbo of forgotten things, and syphilis has continued to flourish like the green bay tree.

Some twenty years ago, reasoning from the perfectly logical premise that mercury is the natural antidote for syphilis, Behrmann of Nuremburg advised anointing the penis with mercural ointment after a suspicious coitus. A few years later, Bonnet of Lyons proposed the use of calomel ointment. Thus it will be seen that not until the twentieth century was a rational prophylaxis developed. The discovery of the causative organism of the disease—the Treponema pallidum—and the fact that animals could be inoculated—a fact that had been denied by such eminent authorities of the past as Hunter and Ricord—led Metchnikoff and his collaborator Roux to approach the question of prophylaxis from the experimental rather than from the empirical standpoint which had hitherto obtained. It is unnecessary to detail the series of experiments on

simian subjects that culminated in the now historic experiment on Paul Maisonneuve. Metchnikoff and Roux proved beyond all doubt that syphilis can be prevented, and their ointment—so simple that it seems most strange that it was not thought of long before—is now in general use throughout the world. The original formula is:

℞—Calomel . . . . . 33 gr.
Vaseline . . . . . 10 "
Lanolin, anhydrous . . . . . 67 "
M.

The ointment should be thoroughly rubbed on the penis and the scrotum within eighteen hours after the suspicious contact.

So efficient did this method prove to be that before the War it was used as a compulsory routine measure of prevention in all of the standing armies of the world. During the War its efficiency was again proven beyond all possible doubt.

Statistics collected by Riggs show that when calomel ointment is used within an hour after a suspected intercourse syphilis can be prevented almost to a certainty—since less than 1 per cent—$\frac{8}{10}$ to be exact—contract the disease. When the application of the ointment is delayed for five hours the number of infections is doubled, that is it rises to 1.57 per cent. If ten hours or more are allowed to elapse before using the ointment the number of infections is 5.14 per cent.

This shows that infection is not instantaneous and it may take from one to several hours before the Treponema pallidum passes through the abrasion which affords its portal of entry into the body beyond the reach of the prophylactic ointment. In those who are so unfortunate as to contract the disease after using the ointment, infection occurs because some part of the penis or scrotum was not protected by the ointment. It is very easy for the physician as well as the layman to understand how this could happen, especially when the ointment has been applied in a hasty and perfunctory manner. Failure to protect is in such instances due to oversight or carelessness rather than lack of protective power of the ointment.

Calomel ointment is now put up in tubes for convenient use and sold in drug stores. Prophylactic packets are also included in the medical stores of the armies and navies of the principal powers, and soldiers and sailors are instructed in the prevention of venereal diseases. Since the War the use of calomel ointment has become much more widespread among the civilian population than previously thereto which is probably due to the knowledge acquired in the army.

I am in accord with Vecki that a most excellent prophylactic measure, and one which persists through life as it were, is circumcision. The indisputable fact that syphilis is less prevalent among

Hebrews than among the uncircumcised Gentiles is ample evidence of this. Circumcision by exposing the glans enables its integument to become transformed into a dermal surface and therefore less liable to abrasions whereby the organisms of the disease can enter. I am convinced that if this simple precautionary measure was universally adopted the incidence of syphilis would be materially reduced.

While individual prophylaxis is of very great importance in preventing the spread of syphilis I am in accord with Pusey of Chicago that by far the most important element of prevention is proper treatment of the disease when it has occurred. By so doing the period of infectiousness is reduced and by reducing the period of infectiousness we automatically reduce the number of those who stand in danger of becoming infected. Under modern treatment the period of infectiousness is materially reduced in comparison to what it was in the old days of mercury and potassium iodide. Arsphenamine not only cures syphilis, it also helps to prevent it.

The academical discussion of the prevention of syphilis and venereal disease in general seems to have a peculiar fascination for some persons, medical and lay. While in some instances such discussion may serve a useful purpose, on the whole it seems to me that not much is gained thereby; this is evidenced by the very palpable fact that syphilis, even if it has abated, has not done so to an extent that it is very noticeable.

Regulation of Prostitution.—The regulation of prostitution with all that it connotes, which is so often injected into these discussions, is not in my opinion a matter for physicians to discuss. It belongs in the domain of sociology and morals, and since this book is a treatise on syphilis as a disease affecting the human body I see no reason why sociology and morals should be discussed here. The prevention of syphilis as a professional problem to the physician I have discussed; and when it is divested of unnecessary and irrelevant side issues it consists in the practical application of the three following propositions:

(1) Instruction through every possible means as to the dangers of syphilis and venereal disease in general.

(2) To those who cannot or will not remain continent instruction as to measures to prevent such disease.

(3) Instruction to physicians through some central source such as the Public Health Service as to the minimum treatment necessary to render a syphilitic free from the possibility of infecting others and a law making treatment compulsory to all those who contract the disease.

The prevention of syphilis and its final extinction are in the hands of the physicians. Better knowledge and better treatment on our part can and will accomplish this.

CHAPTER XLVIII.

SYPHILIS AND LIFE INSURANCE.

It is not my intention in this chapter to deal in statistics, despite the inference that in discussing the subject of life insurance in connection with mortality rates an array of figures forms a necessary part. As Ricord said long ago, "no task is more difficult or more delicate than to apply medical statistics; that, when misdirected or viciously applied, nothing gives rise to greater deception, or to more deplorable error." Be that as it may, statistics have shown life insurance companies the necessity of care in accepting risks that have had syphilis. Moreover the percentage of incidence of the disease has no bearing upon any one applicant, and also the figures of the past are not in harmony with those of the present, that is those that have been collected since the advent of the Wassermann reaction as a diagnostic test. This latter is exemplified by authorities eminent in their day which however, was long before the day of the Wassermann reaction. I will quote the words of Mr. Skey, consulting surgeon to St. Bartholomew's Hospital, London, before a House of Lords committee investigating Contagious Disease Act: "Referring to an article expressing the views of the Association for promoting the extension of the contagious disease acts, it was largely overcharged and colored too highly. The disease is by no means so common or universal as it is represented and I have had opportunity of communicating with leading members of the profession and we are all of the same opinion that the evil is not so large by any means as it has been represented." Many years later, although still before the discovery of the Wassermann reaction, Hyde of Chicago made a somewhat similar statement. He said: "Syphilis is not as has been claimed by a class of hysterical writers, a scourge threatening above all other maladies the devastation of the human family. Tuberculosis annually destroys more victims. . . . The proportion of syphilitic to other diseases in no part of the world exceeds a variation of between 2 and 5 per cent when both sexes are estimated in the statistical returns."

These statements no longer hold. The Wassermann reaction has shown undubitably that syphilis is far more widespread and is the underlying basis of far more diseases than the older clinicians ever dreamed of. We now know, thanks to the modern pathology

of which Warthin of Ann Arbor is the leading exponent, that the Treponema pallidum almost from the beginning of the infection permeates every tissue and organ of the body and especially does it show a prediliction for the vascular and nervous apparatus. It is with the interference of the delicate balance of these two systems that syphilis most frequently shortens life and thus becomes a factor of paramount importance in life insurance. It is in its effect upon the individual rather than its incidence in the mass that I shall discuss the relation of syphilis to life insurance in this chapter. For that reason, I shall dispense with statistics and dwell solely upon the disease as it affects the expectation of life of the individual applicant for life insurance.

Syphilis is usually contracted between twenty-five and thirty years of age in men and about five years earlier in women. Since the disease is undoubtedly of diminished severity in so far as its cutaneous lesions are concerned than it was formerly supposed to be, it is also undoubtedly true that very many persons who have the disease were never aware of having contracted it. These persons therefore, when they deny syphilitic infection do so with absolute good faith. I wish to emphasize this because this happens more frequently than is usually supposed. It is these cases also which form the majority of untreated cases, the reason for which is obvious. Also, it is these cases which show the largest proportion of involvement of the nervous or cardiovascular systems. The mere denial of syphilis even when made in good faith is therefore not to be considered.

Aside from attacking in this occult manner, syphilis may manifest itself more frankly; that is the patient has a chancre which is followed by secondaries such as a macular or papular eruption—usually macular—a few mucous patches in the mouth and then a complete disappearance of all symptoms under treatment, which may be adequate, or, more often, I regret to say, is not. This is the natural history of the majority of syphilitics. While it is true that a large percentage of these never show tertiary lesions that are definitely recognized as such I am convinced that of that number those who have not received adequate treatment form a not inconsiderable percentage of lives that are materially shortened by various visceropathies that can be directly traced to syphilis. Syphilis also attacks in yet another fashion. The patient has a chancre which is followed by secondaries; this time the eruption is nearly always papular. There is more or less alopecia and mucous patches and condylomata lata are present to a marked degree. Otherwise the patient's general health may not be impaired. The lesions whereby the disease is characterized however, are persistent. They disappear only to recur. The disease may follow

this course for a number of years—rarely longer than three, during which time the patient is almost continuously under treatment. If this treatment has been intelligently administered, that is if it has been continuous and vigorous, when the lesions finally clear up they rarely if ever return. In rare instances syphilis may be fulgurant from the onset. That is the lesions even in the early months of the infection may be atrociously destructive and the toxemia engendered by the disease may well nigh overwhelm the patient. Rarely it does so, and syphilis is the primary cause of death. Such cases however, are now most infrequent and need hardly be considered. Malignant syphilis, *syphilis gravis*, galloping syphilis, *syphilis precoce* usually runs a short course. It differs from the usual form of the disease in that its virulence is soon exhausted and when exhausted it rarely if ever revives. Malignant syphilis is hardly ever followed by tertiary lesions. If the disease has spent itself on the osseous and cutaneous structures and spared the nervous system the latter is less likely to be attacked than if the disease had manifested itself in a much milder way.

From this we can generalize that if the disease has been of a mild and ephemeral character or even unrecognized and in consequence thereof treatment has been inadequate or entirely omitted, the possibility of later involvement of the cardiovascular or nervous system or both is much enhanced; whereas if the disease has been severe at the onset and therefore subjected to vigorous and prolonged treatment this later involvement is less apt to occur. This is the consensus of opinion of all syphilologists both before and since the advent of arsphenamine. Since arsphenamine has been added as a therapeutic agent in the treatment of syphilis tertiary lesions at least of the cutaneous and osseous structures have been much less evident. My experience has been, however, that this curtailment of tertiary syphilis does not apply to the viscera such as the heart and bloodvessels, the liver and central nervous system. It has been my experience also that these organs are most apt to be attacked when the disease is otherwise asymptomatic, especially as to lesions of the skin and bones.

The researches of Warthin, McKenzie, Ravaut, Dreyfus, Fordyce and many others show conclusively, as I have discussed at length elsewhere in this book, that this involvement of the nervous and cardiovascular systems occurs extremely early in the course of the disease. In fact it may be said to be almost synchronous with the appearance of the initial lesion. While I am not to be understood as stating that this involvement occurs in every instance of syphilitic infection, or that its presence invariably leads to premature degeneration of the cardiovascular system or to the central nervous system, yet undoubtedly this involvement plus the wear and tear of life is

frequently the determining factor in causing these conditions to appear.

Syphilis is a law unto itself; or rather, it would be more accurate to phrase it that the way that every patient reacts to syphilis is a law unto itself. For it is undoubtedly the patient that reacts and not the Treponema pallidum. It is impossible to determine how the patient will react when infection has occurred. This includes secondary as well as tertiary manifestations and it is the tertiary manifestations with which life insurance is mostly concerned. Syphilis is undoubtedly milder now than it was formerly. I shall not enter into a discussion as to why this is; it is sufficient to say that every syphilologist knows this to be true. Nevertheless it is the most protean of all diseases and the most acute clinician can never foretell what its outcome will be in any given case.

In the chapter on syphilis as a factor in other diseases I have discussed how it can produce or rather simulate—because these conditions when due to syphilis are nothing more than syphilis in disguise—many other diseases, many of which until quite recently were not supposed to have any relationship thereto. But if syphilis produces these diseases it does not produce them any more than, or in some instances as much as, other causes. For that reason with the exception of diseases of the vascular and nervous systems I would discount syphilis. The diathesis induced by tertiary syphilis undoubtedly leads to disease of the liver, the spleen, the pancreas, the kidneys and of the organs of endocrine secretion but as an element to be reckoned with in life insurance I do not think it need be considered. Malignant disease is said to be on the increase and I am not sure but that syphilis may have something to do with it. As a factor of importance however it need not be considered.

From the preceding it is possible to generalize further and to say that is with the exception of nervous diseases and cardiovascular diseases the syphilitic factor, while present, is not present often enough to warrant its being considered as a factor to be regarded as of special importance more so than others in terminal diseases.

As the reader can infer in so far as he has read in this chapter, while by no means disregarding the syphilitic factor in other diseases, I am particular to emphasize the importance of syphilis in causing diseases of the cardiovascular and nervous systems. I do so because I am convinced that the degenerative changes which syphilis so frequently produces in these systems is where its chief danger lies. The predilection of the Treponema pallidum for the walls of the bloodvessels both large and small is a pathologic fact that cannot be denied. This predilection is equally manifest toward the central nervous system—if anything it is more so, as evidenced by the abnormal findings in the cerebrospinal fluid even in the primary

stage of the disease. This tendency to attack the nervous system is still further augmented by the intimate and preponderant influence of the vascular supply of the central nervous system and its supporting membranes, which if attacked independently can alone cause grave changes in the neuro-cellular elements. The Treponema pallidum when lodged in the cardiac musculature may cause no changes therein but it is because of this persistent lodgement in the myocardium that many otherwise asymptomatic syphilitics show a Wassermann-fast serum reaction. Syphilis of the heart, however, is comparatively infrequent in comparison with the changes produced by the Treponema pallidum in the vessel walls. It is the premature arteriosclerosis, with all that this condition connotes, that makes syphilis important to life insurance actuaries. "A man is as old as his arteries" is a medical saw that is a pathologic truism. Aside from accidents and acute infections we last as long as our "tubing" lasts, no longer. Anything therefore which injuriously affects our "tubing" injuriously affects our body as a whole and according to the extent of this injury shortens our lives. Such an eminent clinician as Lewellys F. Barker of Baltimore is of the opinion "that syphilis especially has been much overestimated as a causal factor in chronic arterial hypertension." This is true if we go to the extreme as some have done to attribute every case of hypertension of the arteries in persons under fifty years of age to syphilis. But I do not hesitate to say, and to say so because I am profoundly convinced of the truth of it, that syphilis more than anything else is the cause of hypertension in men under forty-five years of age. I am in full accord with Barker that when this hypertension is slight it need not cause alarm and that such patients with proper care may live their alloted span; yet as insurance risks they should be accepted with caution, knowing as we do the ultimate results in the majority of cases of high blood-pressure.

Like the infiltration of the vessel walls due to the irritant presence of the Treponema pallidum therein, syphilitic disease of the nervous system is equally slow and insidious in its development. Aside from the coarse paralyses sometimes occurring in secondary syphilis the two most devastating forms of syphilis of the nervous system are of extremely slow evolution—I refer to tabes dorsalis and paresis. Both of these diseases are on the increase. I am not in accord with Kirby that they are decreasing. While tabes may allow life to continue for many years, no life insurance examiner would possibly accept a potential tabetic or paretic.

I shall not discuss the influence of syphilis superimposed on pathologic conditions already existing; if they are diseases with a lethal termination they would automatically cause the refusal of the risk even in the absence of syphilis and therefore they have no bearing on the matter under discussion.

Congenital syphilis rarely has to be considered in life insurance. The majority of congenital syphilitics show a negative Wassermann reaction after eighteen years of age. The former presence of the disease can usually be recognized by dystrophies that to the trained observer are very patent. As a rule the progeny of syphilitics even if they survive the pathologic vicissitudes of infancy and childhood rarely develop into robust men and women. As insurance risks they are usually below par, although exceptions are often seen. Adults of congenital syphilitic antecedents are particularly prone to tuberculosis and this tendency is usually sufficiently evident physically to preclude their acceptance as risks.

From what I have said in this chapter in regard to syphilis and life insurance the reader can readily infer that I have very definite ideas on the subject. Definite though they are, and perhaps somewhat dogmatically expressed, yet when analysed by the cold logic of reason based upon acknowledged facts they cannot be controverted. In order that the reader may the better survey the conclusions which I have expressed in this chapter and also in other chapters of this book in so far as the matter contained therein can be referred to syphilis and life insurance I will summarize them as follows:

It is difficult to arrive at a definite opinion as to the incidence of syphilis among civilized peoples. In the United States probably about 10 per cent of the white population is syphilitic; among the negroes it is probably twice or thrice this percentage. Syphilis for very obvious reasons is more prevalent among those dwelling in cities than it is among those dwelling in the country. I am of the opinion however that, for some time to come this discrepancy will not be so noticeable owing to the war. I am also of the opinion that for some years to come the incidence of the disease will be greater than it was before the catastrophic calamity. That it is more prevalent among the better or more educated classes (as Kolmer asserts), I do not believe. It was formerly believed that syphilis was not as prevalent as we now know it to be since the Wassermann reaction as a diagnostic test came into use. Neither was it known as we now know it to be the basis of so many diseases, frequently of a fatal type, that are usually considered independent of syphilis as a causative factor.

Syphilitic infection can occur unknown to the person infected and may exist for years without exhibiting any symptoms which would enable its presence to become known. Therefore the denial of infection by an applicant made in good faith is no evidence that the disease is not present. For that reason the only logical way to determine whether the disease is present or not in an applicant is to make a Wassermann test of his blood. In order to arrive at a correct estimate concerning this serological reaction it must be

known that the applicant has not eaten within five hours of taking the blood and has abstained from alcohol for three days previously.

Syphilitic infection that has been attended with moderate or severe lesions in the early or secondary stage, providing that they did not involve the nervous system, and which received energetic and long continued treatment, is less liable to develop tertiary manifestations than the infection that was seemingly transitory or so slight as to pass unnoticed, and in consequence thereof received treatment that was merely palliative in so far as causing these symptoms to disappear, or no treatment at all. All other things being equal the applicant whose early syphilis has been severe but who has received adequate treatment for the same is a better risk than the applicant whose early syphilis was slight or asymptomatic and who was treated accordingly. An applicant who has shown tertiary manifestations of the disease within five years of applying for insurance should in my opinion, be rejected unless he can satisfy the examiner that he has had adequate treatment within that time and his Wassermann reaction has been negative for two years. If such be the case he can be accepted at an advanced rate, or for a limited payment policy also at an advanced rate. Early moderate or severe syphilis, that has been well treated and that has had no tertiary recurrences should not, in my opinion be a bar to insurance. If the Wassermann reaction is still positive a sharp advance in the rate or a limited payment policy should be the terms of acceptance. If ten years or more have elapsed since the date of the infection and the Wassermann reaction is found to be negative the risk may be accepted at the usual rates or at a slight advance thereon. The applicant with no somatic signs of the disease except a positive Wassermann reaction and who denies infection because of the ephemeral character of the primary or secondary lesions, should *not,* in my opinion be accepted. It is these cases beyond all others that most frequently develop tabes and paresis and arterial hypertension.

Applicants for insurance with a history of syphilis either admitted or discovered through the serological test, who show arterial hypertension even to a slight degree should be rejected.

The elimination of risks that will later in all probability develop syphilitic disease of the nervous system—tabes and paresis in particular—is from the standpoint of the life insurance examiner extremely difficult; although from another standpoint this possibility can be easily determined. The presence of spinal miosis, Argyll-Robertson or other pupillary anomalies, lost, unequal or exaggerated reflexes are easily ascertained, and an applicant in whom these signs are present should be unqualifiedly rejected. But the long premonitory stage in which these pathognomonic signs are

entirely absent can only rarely be clinically detected even by the most acute diagnosticians. It can be infallibly detected however by a comparatively simple measure—lumbar puncture. This diagnostic measure would be extremely difficult to apply as a routine in examining for life insurance. It need not therefore be further considered. Lumbar puncture for the purpose of examining the cerebrospinal fluid to determine the completeness of a cure is gradually, however, becoming a regular procedure among advanced syphilologists and clinicians generally. As it comes more and more into use, and intraspinal therapy is employed more frequently and earlier than it now usually is, I am convinced that the incidence of these degenerative diseases of the central nervous system will become correspondingly reduced.

Syphilis undoubtedly shortens life; for that reason more or less caution should be exercised in accepting a risk known to have or to have had the disease. If, however, the postulates laid down in this chapter are carried out in regard to such risks, the losses therefrom will be brought to the irreducible minimum.

CHAPTER XLIX.

SYPHILIS AND INDUSTRIAL EFFICIENCY.

Efficiency engineers have more and more realized the factor of disease in lowering industrial efficiency. The disease that has been most studied in this regard has been pulmonary tuberculosis but the lessons taught by the World War and which to a certain extent were glimpsed even before, have led them to include syphilis in the category of diseases which diminish working capacity both in quality and output. Not that there is any trade which is conducive to contracting syphilis, for there is not, with the possible exception of glass blowing; but because syphilis in many of its phases, by incapacitating the workers, reacts upon industry. The incidence of syphilis therefore becomes an economic factor of more or less importance. This importance may be said to be more rather than less because of the wide incidence of the disease and its known crippling effects in many instances. For the same reasons that it was sought to eliminate alcohol so now it is attempted to eliminate syphilis. This preservation of the worker's health has a direct ratio to his efficiency and shows a tangible evidence in dollars and cents. It is a policy therefore which is not only humane but which is also wisely selfish. The hand (which Aristotle called "the instrument of instruments") that is part of a healthy body does better work and more work than that which is part of a diseased body.

In so far as preventing the evil effects of syphilis the words of Patrick Henry would apply most strongly: "The price of liberty is eternal vigilance." The only way to prevent its ravages is to be constantly on the watch for the first signs of its insidious attack. Before discussing how this can be done—and it can be done—I shall point out briefly wherein syphilis is an ever present menace to industrial efficiency. By so doing I believe the importance of combating it will be better realized by those most interested—the employers of labor in large quantities.

In its earliest stage—that is the stage of the chancre—it is only by the widest stretch of the imagination that syphilis can be said to affect individual efficiency. This statement may be modified however, to the extent that the mental shock of having acquired the disease in a few imaginative and highly-strung individuals may

produce a frame of mind that would interfere with their efficiency. While this may be classed as an "imponderable," yet it is undoubtedly true in some instances. I am firmly convinced that not a few suicides are due to the discovery that syphilis has been acquired.

In the secondary stage also syphilis rarely has a deteriorating or incapacitating physical effect. There are important exceptions to this however, if we consider the paralyses, and inflammations of the eyes which occur in this stage.

In the tertiary stage from the standpoint of industrial efficiency we have to consider such destructive diseases as paresis, locomotor ataxia, chronic heart disease, including aneurysm and hypertension, diseases of the liver and other abdominal viscera, endocrinic diseases and diseases of the bones. In other words, as I. have discussed elsewhere syphilis can bring about almost any disabling or life-shortening disease.

When we consider that syphilis is usually contracted between the ages of twenty-five and forty years, and the tertiary manifestations mentioned usually develop within ten or fifteen years thereafter, it will be seen that disability resulting therefrom occurs most frequently during the period of highest economic productivity, that is between the ages of thirty-five and fifty. Syphilis therefore is most apt to injure the capacity of the skilled man—the man of the highest economic value.

That this is a real and present danger is proved by the widespread incidence of syphilis. From estimates made before the War, Gerrish estimated that 10 per cent of the population of the City of New York was syphilitic. Fischer estimated the total syphilitic population of the United States to be approximately 18 per cent. This also was before the War. Subsequent to that catastrophe I am inclined to place the percentage of those infected with syphilis considerably higher. So that for the next ten to twenty years at least syphilis as a disabling factor will be increased rather than decreased.

Now as to the measures to be employed whereby this great and undoubted economic loss can be prevented. Can it be done? To this question I would answer emphatically in the affirmative. It can. For a number of year it has been customary for most large employers of labor to maintain a medical staff whose duty it is to look after the physical welfare of their employees. The medical staff as now constituted examines applicants for work to detect disabilities for certain kinds of work, and treats or recommends certain forms of treatment to those employees who apply to them either voluntarily or under direction. I know of no instances where the medical staff investigates or treats for syphilis. Yet these physicians should know (if their employers do not), that 20 out of every

100 of their workmen—and this includes the highest executives as well as the humblest and most unskilled laborer—have syphilis—and syphilis frequently masquerades under pathologic symptoms more euphonious than innocent. They also know that tertiary syphilis—especially of the central nervous system—is of most insidious approach—and if it is to be prevented with any degree of success it should be attacked at its earliest onset.

All this being known—and there is not, I venture to say, a physician on the staff of any individual concern throughout the land who does not know it—there are two measures which can and should be used to prevent the personal disasters which by reaction entail diminished industrial efficiency and consequent monetary loss. One is to take a Wassermann test of every employee before he enters employment and periodical Wassermann surveys thereafter; this would also include a clinical neurologic survey with the possible addition, if the facts in any given case warranted it, of an examination of the cerebrospinal fluid. The other measure is prompt and efficient treatment of all cases which require it.

Divested of detail and of circumlocution, it is all that would be required to prevent, or rather to reduce to the minimum the losses that are caused by syphilis. It is not a problem impossible of solution or fraught with grave difficulties. On the contrary it is extremely simple. It may be objected to in certain quarters as meddling paternalism or industrial feudalism, but I am quite sure that it cannot be objected to as not being "good business."

A latent and apparently asymptomatic syphilitic infection can undoubtedly be activated by trauma. Under such circumstances the legal question arises whether the syphilitic claimant can collect damages from his employer or other for a disability arising from his disease but actually caused by an injury received while employed or otherwise. In such cases the claimant may show very conclusively that the lighting up of the disease was due to the injury. Conjecture or surmise on the part of the physician cannot be accepted by the court. In this regard I would call especial attention to injuries of the head which may precipitate paresis. Such injuries can undoubtedly do this, but the claimant would experience extreme difficulty in proving his case if the paresis developed later than three months succeeding the injury.

CHAPTER L.

SYPHILIS AND THE LAW.

The ideas of most physicians in regard to the existence of communication of syphilis from the legal point of view are, to say the least, extremely vague. Such relation, however, does exist, and the facts pertaining thereto should be known. Especially is this true of syphilis and marriage, for it is concerning this relationship of the disease that the physician is most frequently consulted.

The introduction of syphilis into the marriage relation entails physical injury to the unaffected partner and also to any children which may be born to such a union. For this reason, therefore, the communication of syphilis by one partner to the other, or even the exposure of one partner to contagion from the disease, may affect (1) contracts to marry; (2) annulment of the union; (3) divorce.

In most instances the physician is called upon to determine if it is safe for a syphilitic man to marry. If he decides that it is not the majority of men will heed his advice and defer the proposed union until such time as the medical adviser may deem it safe so far as transmitting the disease to his prospective wife and to any offspring, which may follow, is concerned. There are some men, however, who for reasons best known to themselves do not care to follow the advice thus given, and in these cases the physician, in order to avert consequences which may be disastrous, must impress upon the unwilling one the legal consequences involved in transmitting his disease to his wife. Again, the physician may be consulted by a married woman who has been infected by her husband and who, in consequence, is determined to live with him no longer.

In order that the physician may advise intelligently in a situation of this kind—a situation, I may add in passing, which sooner or later confronts every physician in active practice—he should have some knowledge at least of that branch of forensic medicine which pertains to syphilis and the marriage relation. He should be acquainted with what the law accepts as valid grounds for divorce, what must be the concurrent conditions for its intervention, as well as the attendant disadvantages to the complainant, which are inseparable to a suit for a divorce in which syphilis is the cause of action.

Let us first consider what redress the law affords to a woman who

has been infected by her husband with syphilis. In the first place it must be observed that the mere existence of a venereal disease—and syphilis is so considered in this discussion—in one partner, or even its communication by one to the other, does not *per se* constitute sufficient ground for divorce. The law requires that there must be certain concurrent conditions of an aggravating character, the existence of which must be proved. In no civil code is venereal disease specially mentioned as a statutory ground for divorce, nor is there any penalty laid down for its transmission. The nearest approach to it is to be found in the civil code of Kentucky, in which it is stated that the contraction of a "loathsome" disease by one of the partners is a specific ground for divorce, and it has been held that any venereal disease is to be included under the term of "loathsome."

This absence of legislation in regard to the transmission of syphilis in the marital relation may at first sight appear as a failure of the law to recognize the grave physical and mental injury, which may result from such transmission of the disease. If syphilis were a disease that was exclusively venereal, that is if it were invariably transmitted by sexual embrace, either before or after marriage, there would undoubtedly be grounds for criticism for this seeming oversight. But, as is well known and is recognized by the law, syphilis may be contracted in a manner wholly innocent and it may be transmitted by one partner to the other in a manner also wholly innocent. This being the case, if the law specifically decreed that one partner might demand a divorce because of syphilis communicated by the other, the strict construction of such a law might cause a grave miscarriage of justice in some instances. For example, if a wet nurse acquired the disease from suckling a syphilitic infant and communicated the disease to her husband, she might be completely ignorant of the nature of her disease and could not be held either morally or legally responsible. In cases of unconscious communication of syphilis acquired in an innocent manner, the conjoint who transmits the disease is legally and morally exonerated.

Fournier has recorded a case of a physician who contracted a chancre of the tonsil after having put in his mouth a paper cutter, which he had previously used as a tongue depressor in examining the throat of a patient. The nature of the lesion was not recognized and he communicated syphilis to his wife. The aw cannot foresee or provide against these possible contingencies, and it perhaps wisely includes the offense under some general, rather than under a specific, statute.

While the principles which underlie the decisions rendered by different tribunals are practically the same, the rulings are by no means uniform and often appear contradictory. This is not surpris-

ing, however, if we consider the varying circumstances and accessory conditions which complicate the transmission of syphilis in the marriage relation. In some instances the circumstances are held to aggravate and in others to mitigate the culpability of the offender, and these must all be taken into consideration and given due weight in arriving at a decision, special cognizance being always given as to whether the act was committed knowingly and wilfully.

It is generally held by the American and English courts that the communication of syphilis constitutes cruelty if it can be proven that it was wilfully and knowingly transmitted. Cruelty in England, and in many States of the Union, is a sufficient ground for divorce. In France the Code Napoleon provides that one partner may demand a divorce on the ground of "grave injury," and since the communication of syphilis is held to be grave injury inflicted by one partner on the other, proceedings may be instituted on this ground with the added one as a natural corollary of infidelity. The civil codes of nearly all civilized countries recognize infidelity as sufficient cause for divorce, and if this charge can be proven the graver physical injury of syphilitic infection is usually passed over in silence.

Syphilis a Defense in Breach of Promise.—The existence of syphilis in either party to a contract to marry is sufficient reason for the other party to refuse to fulfil the engagement and, therefore, establishes a valid defense in a breach of promise suit. Although this point has not been judicially determined in England, it has been laid down as a general rule that if the condition of one of the parties thereto was changed after making the contract it was sufficient ground for either to break the engagement. Few actions for breach of promise have been brought in which this defense was set up. This line of defense on the part of the male contracting party would be enough to induce any respectable or self-respecting woman to discontinue the suit. Such cases, however, have come before the courts in this country for adjudication where the defendant in a breach of promise suit refused to marry the plaintiff by reason of a venereal disease in himself.

In such cases the law is that where a venereal disease is contracted prior to, but not known to exist at the time the contract to marry was entered into, or if such disease was contracted subsequent to entering the contract, but through no wrongful act on the part of the defendant, the existence of such a disease furnishes a good defense for an action for breach of promise to marry.

In a ruling given by one judge the following statement was made: "We cannot understand how one can be liable for not fulfilling a contract when the very performance thereof would in itself amount to a very grave crime not only against the individual but against society itself. . . . The law will constrain no man to assume a

position so full of peril as to place within his reach the lawful means of gratifying a powerful passion at the risk of another's health and life, and the possibility of bringing into the world children in whose constitution the seeds of a father's sins shall lurk."

Syphilis Renders Marriage Voidable.—The existence of syphilis in either party at the time of the marriage may render the marriage voidable. In other words, annulment of the union may be sought for and obtained on this ground. In such cases the annulment would rest upon the ruling which recognizes permanent and incurable impotency as a sufficient ground for divorce. In construing it to apply to syphilis, the ruling rendered was that "while there was no such malformation which renders complete sexual intercourse impossible, there was a physical reason that rendered her (the defendant) incapable of healthy coition. Every such act, by reason of her physical condition, was attended with great danger of communicating to him incurable disease and endangering his health and life. . . . In the case at bar the petitioner's organs of generation were at the time of marriage in an incurably diseased condition, which, while it did not physically render her incapable of copulation or of bringing into life a child with a mass of syphilitic sores, as good as dead when born, yet it did render copulation and procreation on the part of the petitioner impracticable, because the act endangered both his health and life."

In a case decided in New Jersey the marriage was annulled on the ground of "fraud." The man had syphilis, although he had assured his intended wife that he never had any venereal disease. When his deception was discovered she brought suit for the annulment of the marriage. The court held that "to annul a marriage for a fraudulent representation inducing the contract it must be shown that the fraud affected an essential of the marriage. An explicit statement by a man about to be married that he was not affected by the loathsome disease called syphilis, made when it was his duty to state the truth, and knowingly false, is such a fraudulent representation as affects an essential of the marriage relation."

"The decree cannot be had upon the uncorroborated evidence of the complainant. The contract of marriage is one of exceptional and peculiar character. On the grounds of public policy the State has an interest in the status created by a marriage contract, and when made it can only be dissolved on grounds and by judicial proceedings sanctioned by law."

In this particular case it was proven by the testimony of the physician who had treated him that the man had syphilis and was informed of the nature of his disease.

In another case, in which action for the annulment of the marriage was instituted by the wife on the ground that the defendant was constitutionally affected with syphilis and was aware of the fact

at the time he married her, but failed to inform her of the fact, upon becoming acquainted with the fact and before sexual relations were entered into, she left him and refused to live with him. In this case the court held that "his concealed disease was such as would leave him with no foundation upon which the marriage relation could properly rest; that the libellant could not live with him as his wife without making a victim of herself for life and giving her offspring, if she had any, an inheritance of disease and suffering. Few, if any, would be bold enough to say that it was the duty of the libellant on discovery of the fraud before consummation of the marriage, to give herself up as a sacrifice and to become a party to the transmission of such a disease to her posterity."

In another case annulment was decreed, although the parties had continued to cohabit after the nature of the defendant's disease became known to the plaintiff. It was expressly held that such continuance of cohabitation could not be regarded as condonation.

Huberich writing on "Venereal Disease in the Law of Marriage and Divorce" in the American Law Review states: "To constitute a ground for cruelty it is usually required that the disease should have been actually communicated to the complainant; that the complainant should have been ignorant of the existence or nature of the plaintiff's disease at the time of its communication, and that the defendant should have infected the petitioner knowingly and wilfully. If all these facts concur, no question of the propriety of granting the divorce can arise unless there are facts showing condonation of the offense."

The weight of authority is that the disease must be actually communicated. In one decision it was held that "attempted intercourse with the complainant when defendant was afflicted with a contagious disease would suffice to sustain a charge of cruelty."

In still another decision it was held that "a reasonable apprehension of injury is sufficient, and the complainant need not wait until the wrongful act is committed."

Justice Key, in a case before the Texas Court of Appeals, states: "A man may, as a result of his own debauchery, become so diseased as that living and cohabiting with him will probably destroy the health of his wife, and we are not prepared to say that such fact would not, of itself, entitle a pure and innocent woman to a divorce, in the absence of specific proof that he had communicated to her a loathsome venereal disease."

In the courts of this country, stress is laid upon ignorance of the existence or nature of the disease on the part of the complainant. In one case in which the wife was informed of the disease of her husband, and of its contagious nature, but continued for a year and up to the last moment of their living together to submit willingly to his embraces, was denied a divorce.

But where the complainant is ignorant of the nature of the plaintiff's disease, no case of waiver or condonation arises. A divorce was granted to the woman in a case where her husband had communicated syphilis to his wife, but had ascribed her syphilitic angina to drinking from an infected cup and had continued marital relations with her.

In the French courts no stress is apparently laid upon this point, as it is hardly to be assumed that a woman would marry a man knowing him to be syphilitic. The French tribunals consider the transmission of syphilis in marriage a grave injury and, therefore, a cause for separation, whether the husband has contracted the disease before or after marriage. The mere fact that the conjoint is exposed to the contraction of the disease when the husband is aware of the disease and its contagious nature, is allowed in France as a sufficient ground for divorce.

The law lays especial stress upon whether the disease is communicated knowingly and wilfully. If the defendant believes himself cured at the time the infection is alleged to have taken place and the court decides that the defendant's statements in this regard are entitled to credence, he is not guilty of cruelty.

The "concurrent conditions" upon which decisions are based are practically the same in all courts of justice. There are certain circumstances, however, which are held to aggravate or extenuate the charge of cruelty or grave injury. The responsibility of the husband is increased when he has made no attempt to repair the damage to his wife's health by securing proper medical treatment or if he has sacrificed her health because of a feeling of so-called false shame. On the other hand it is regarded as a mitigating circumstance if the husband has employed every means at his command to secure for the injured party proper and efficient treatment.

From this survey of the jurisprudence of syphilis and marriage it appears that when a woman has been infected with syphilis by her husband the law may grant her a divorce on the statutory grounds of cruelty or infidelity. In the State of New York, wherein this is written, infidelity alone is recognized as the sole ground for an absolute divorce and, therefore, the charge of cruelty could not be pleaded.

Under the present conditions of the law, the physician should advise his patient that syphilis should never be invoked as a cause of action for divorce unless it constitutes the principal or only phase of cruelty that can be alleged. The charge of infidelity, if it can be sustained, should always be the preferential plea. Under such circumstances it is wise to advise that syphilis should not be brought forward as a prominent feature in such an action as it will not affect the result if infidelity can be proven, and it will be ignored by the trial judge. Furthermore, if the fact is pleaded and established

publicly in court that a woman is the victim of a loathsome disease, which is by many regarded as incurable and transmissible to her offspring, even if she is successful in gaining her suit on these grounds she will be stigmatized, although she be innocent, as the bearer of a shameful disease, and her children, if she have any, may also have to carry this stigma through life, greatly to their future detriment.

For this reason, if no other, the woman who seeks a divorce upon the ground of syphilitic infection by her husband should be advised most thoroughly of the ordeal she must face. In the first place, she must furnish legal proof that she has syphilis and that she acquired it from her husband. While the existence of syphilis in the wife may appear as *prima facie* evidence that she contracted the disease from him, it is still by no means absolutely conclusive in the eyes of the law. Therefore, she must prove (1) that her husband has syphilis; (2) that she has syphilis; (3) that the syphilis of her husband has been transmitted to her. She will be called upon to reveal secrets of private life, often disgusting and shameful in their nature. She must also be prepared to face the inevitable scandal and publicity. She must appear in court or before a referee and testify concerning experiences which are not always kept from the newspapers. Even if successful she will find that she has purchased her freedom at the price of humiliation and shame.

In regard to the physician's line of conduct in the matter of syphilis and divorce, it is rarely advisable that he should appear in the interest of his patient. The proof of the communication of the disease can be furnished by a medical expert appointed by the court for the purpose of making an investigation. Especially should the attending physician *not* give a letter or certificate stating that the woman has syphilis and that he is treating her for the same. Certificates of this character are often looked upon with suspicion and have even been rejected by the court.

Syphilis is sometimes brought forward by the defendant in breach of promise to marry. In this connection I will quote opinions that will elucidate the law in regard to such actions. In February, 1882, the Supreme Court of North Carolina decided in the case of Allen *vs.* Baker that if the defendant contracted the disease subsequent to the time of making the promise to marry, or, if before, and he knew, or by extraordinary diligence could have known, that his infirmity was incurable, he would be held answerable; but if it was contracted prior to the promise and he had reason to believe that it was only temporary he would be excusable.

An interesting case was that of Hamilton *vs.* Schackelford, tried in one of the Circuit Courts of Kentucky in July 1890, and from thence carried by the defendant to the Court of Appeals.

In this case, the engagement to marry was entered into in December 1887. The defendant alleged that prior to entering into the

engagement he had contracted syphilis but that he had been treated by a physician in good standing until he had been advised by his medical attendant that he was free from the disease and could safely enter into the marriage relation. Believing this he entered into the contract in good faith with the plaintiff. Since that time, and through no fault of his, the disease had reappeared upon him. Upon the advice of his physician that his condition rendered him unfit to marry—that the disease was still in his system—and that it would be communicated to the plaintiff in the event that he made her his wife and availed himself of his conjugal rights, he broke the engagement.

The Circuit Court adjudged this defence not good and sufficient upon demurrer, but permitted defendant to plead the same in mitigation of damages. The case went to a jury and the plaintiff was awarded $4500 damages. The defendant thereupon carried the case to the Court of Appeals which reversed the judgment of the lower court and held that the answer of the defendant presented a good defense and bar to the action and excused the defendant from the performance of his contract to marry the plaintiff.

The principle of law established is that if a man who once had syphilis believed, as so advised by a reputable physician, that he was free from the disease and was in a condition to marry, should enter into an engagement to marry and during the engagement there was a reappearance of the disease, through no fault of his, which would endanger his future wife, he would be released from his contract and relieved from any liability for damages because of such refusal.

The first State to pass a law requiring that all cases of venereal disease should be reported by name direct to the State Board of Health was Vermont. This law went into effect in 1915. New Jersey passed a similar law in 1917. For many years strenuous objections to the enactment of such laws were made on various grounds, but while it is realized that the confidential relation that exists between the patient and the physician must be maintained, yet a knowledge of the prevalence of these diseases, in order to estop them as much as possible, was absolutely necessary. Slowly but surely these objections have been answered and overcome so that now the number of States which have such laws on their statute books is increasing year by year.

In the State of New York systematized efforts to control the venereal peril have been made for a number of years. Although progress may seem slow, yet they are bearing fruit. In May, 1917, was enacted that part of the Domestic Relations Law, Chapter 25, which provides that applicants for license to marry must make affidavit that: "I have not to my knowledge been infected with any venereal disease, or if I have been so infected within five years I have had a laboratory test within that period which shows that

I am now free from infection from any such disease." This was the first effort to legally control venereal disease—feeble and inadequate though it is. The next measure was Regulation 29-A of the Sanitary Code, which mentioned syphilis and gonorrhea as dangerous diseases and made provision for furnishing information through circulars distributed to those interested. Another law enacted, which has helped much to diminish the ravages of venereal diseases, is the Advertising Law, Section II, 42-A, which aims to control the practice of quackery which in a great city like New York had grown to huge proportions.

The next regulation in the effort to control venereal diseases was in the form of an amendment to the Public Health Law in regard to reporting communicable diseases. This went into effect on April 10, 1918. This amendment is a part of Chapter 177, paragraph 25, and reads as follows: "Whenever an examination for diagnosis by a laboratory or by any person other than the physician in charge of the person from which the specimen is taken discloses the existence of a case of infectious and contagious or communicable disease, the person in charge of such laboratory or the person making such examination shall immediately report the same, together with all the facts in connection therewith, to the Health Officer of the city, town or village from which such specimen came, and shall keep a permanent record of all the facts in connection with such examination, including the identity of the person from whom the specimen is taken and the name of the physician, if any, sending such specimen."

An amendment to the Sanitary Code which became effective on August 1, 1918; Chapter II, Regulation 2-A, provides for reporting cases of communicable diseases by physicians and for submitting specimens for laboratory examination in cases of syphilis, gonorrhea and chancroid.

Chapter 264 of Health Legislation added two new sections—343—M and 343—T, which confer upon health authorities the power to examine any person reasonably suspected of being infected with a venereal disease and provide for the isolation and treatment of such persons.

Another new law in Health Legislation is Chapter 342, which was passed on April 30, 1918. This law provides for the creation of a Bureau of Venereal Diseases in the State Department of Health. By this measure the Bureau is authorized to buy, manufacture and dispense remedies for the treatment of venereal diseases, to examine specimens submitted to it, to provide and distribute literature and to use such other means as might seem desirable for the instruction of the public. Article 17—B of Chapter 264, section 343—O, requires persons with venereal disease to comply with the rules and regulations approved by the Board of Health or Health Officer of

the district in which such person resides. This section also makes provision for carrying out further details of isolation and treatment.

The right of local health authorities to quarantine a person, known to be infected with a venereal disease, has been upheld in the courts. I quote: The Supreme Court of Nebraska, in a recent case, ex-parte Brown, upheld the right of local health authorities to isolate a person infected with venereal disease. A woman was arrested and upon examination was found to be infected with a venereal disease. The Health Commissioner of Omaha ordered her to be detained in the detention home of the city for treatment until there was no further danger of her communicating her disease. In a habeas corpus proceeding to procure her release the court upheld the action of the Health Commissioner and denied the writ. The opinion read: "In this case the stipulation shows that the petitioner was found to be infected with communicable venereal virus and that she was only detained for such reasonable time and in such reasonable manner as to prevent the danger of said petitioner from communicating such infection to others and until the danger of the infection shall be removed."

The right to restrict the liberty of persons suffering with certain infectious diseases such as syphilis and gonorrhea and chancroid—the venereal triad—is today everywhere admitted. The havoc wrought by "Typhoid Mary" exemplifies this. There is no reason why the community should be exposed to such insidious dangers on the plea of maintaining personal liberty. There is no principle of personal right involved. It all resolves itself into a question of expediency to protect society. Every community has the inherent right to protect itself. Restrictions, therefore, applied to carriers of disease, be it the Bacillus typhosus or the Treponema pallidum, are perfectly right and proper and are to be considered solely on the basis of community welfare and not on that of individual pleasure, profit or convenience.

CHAPTER LI.

THE MANAGEMENT OF A SYPHILITIC CLINIC.

THERE are few if any hospitals with clinics attached for the treatment of ambulatory patients that do not have a genito-urinary or dermatologic clinic. With very few exceptions the patients with syphilis are treated in either one of these. Furthermore the syphilitic patients treated as such are only those in whom the evidences of the disease are very plain—an initial lesion, or an eruption. The large number of patients with syphilitic nervous disease, or with syphilitic visceropathies are treated in the department of nervous diseases or in whatever department includes their special ailment without considering whether that ailment has an underlying syphilitic basis or not.

Recognition of Syphilitic Patients.—Since syphilis is such a prevalent disease and its presence is often masked under pathologic entities with more euphonious names, every patient coming for treatment for any chronic condition, be that what it may, should undergo a Wassermann test of the blood. By so doing the underlying cause of many obscure conditions will be recognized and also the prevalence of syphilis in a community can in a measure be determined.

The taking of the Wassermann reactions should be under the control of the department of syphilis which thus acts as a clearing house for the other departments in so far as separating the syphilitic from the non-syphilitic is concerned. This also affords a better opportunity for the study of the syphilitic factor in other diseases—a factor which, I may say, is coming to be recognized more and more all the time. The presence or absence of syphilis will thus automatically determine whether a patient comes under the department of syphilis or not.

Staff of Clinic.—According to the size of the service the department of syphilis should have a chief, whose word in matters of diagnosis and treatment should be final, and as many assistants as necessary. The junior of these assistants should be designated as clinical clerk.

Examination.—When a patient presents himself his history should be taken and then he should be passed on for physicial examination either to the chief of some assistant assigned to that

detail. It is best to have the patient examined by several men each being assigned to some special detail in that regard. Each should mark his findings on the history sheet. This should include the examination of the chancre if present, the surface of the body for evidences of skin eruptions or other cutaneous lesions, the examination of the heart and lungs, the reflexes and an ophthalmoscopic examination. A sample of urine should also be taken and lastly blood should be withdrawn for a Wassermann test—this should never be omitted. In cases where there is some interesting lesion or dystrophy capable of being photographed, this should be done if possible.

In this way the patient is subjected to a thorough and coördinated examination and the clinical facts tabulated so that in time statistical material of great value will be accumulated.

History Sheet.—The following is a sample of the history sheet used in my service in the hospitals of the Department of Correction of the City of New York.

HISTORY SHEET.

Name———.....

Age..———.....Married or single———.....

History:

(*a*) Past illnesses:

(*b*) Present illness.

Dermatologic:

Cardiac:

Pulmonic:

Reflexes:

Urinalysis:

Wassermann (date of first and subsequent tests):

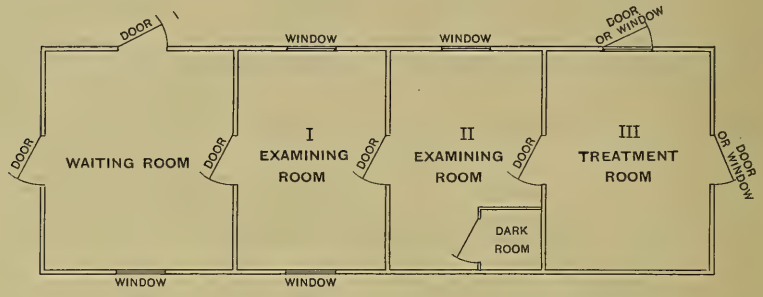
Treatment:

Results of treatment:

If, while the patient is under treatment for syphilis some other condition should arise, the patient should be referred to the department under which such condition would come and the fact entered on his syphilitic history sheet. The syphilitic clinic should be for syphilis only.

Arrangement of Rooms.—In so far as the arrangement of the clinic rooms is concerned I can understand that it is not always possible

to have an ideal plan, nevertheless if good work is to be done there must be at least some attempt to attain this ideal. The rooms should be light and well ventilated and of size ample for the work required. The plan submitted here will, I think, meet these conditions.



It is to be understood that the plan here given is strictly tentative, but it gives at least an adequate idea as to how the rooms of a clinic for the exclusive diagnosis and treatment of syphilis should approximately be arranged. The waiting room can be dispensed with—it is not necessary if there is a general waiting room. In the treatment room there should be a door that will allow the patient after treatment to pass out without coming in contact with the patients undergoing examination or awaiting treatment. I do not deem it necessary to dwell upon the equipment of the treatment or operating room. The question of equipment is a matter of resources in so far as the institution maintaining the clinic is concerned; and much of it will depend on the individual choice of the syphilologist in charge. It goes without saying that this will be in accord with modern standards.

Fees.—I am strongly in favor of charging a fee of a dollar or so in advance, of the cost of the arsphenamine, as this additional charge will enable the clinic to be self supporting—a most happy state of affairs when we consider how often hospitals are pressed financially. It also helps the patient to maintain his self respect which is a desideratum that should not be overlooked.

These few, brief suggestions as to the management of a syphilitic clinic are not intended to be in any way dogmatic. They are, I may say, of a very general nature, and are intended more to give an idea than a concrete plan. No one realizes more than I do the verity of the old saw "circumstances alter cases;" and no one realizes more than I do how circumstances alter the planning and conduct of a clinic—especially for syphilis.

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